L Number	Hits	Search Text	DB	Time stamp
1	2	"bacteria-to-bacteria"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 17:13
-	22	plasmid same bacteria same gene same transfer$ same prevent$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 14:22
-	1	(plasmid same bacteria same gene same transfer$ same prevent$) and taurolidine	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 14:34
-	1	"bacteria-to-bacteria transfer"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 17:13

```
=> file caplus wpids biosis medline embase

FILE 'CAPLUS' ENTERED AT 17:22:41 ON 19 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 17:22:41 ON 19 FEB 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'BIOSIS' ENTERED AT 17:22:41 ON 19 FEB 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'MEDLINE' ENTERED AT 17:22:41 ON 19 FEB 2003

FILE 'EMBASE' ENTERED AT 17:22:41 ON 19 FEB 2003
COPYRIGHT (C) 2003 Elsevier Science B.V.  All rights reserved.

=> d his

     (FILE 'HOME' ENTERED AT 17:22:04 ON 19 FEB 2003)

     FILE 'CAPLUS, WPIDS, BIOSIS, MEDLINE, EMBASE' ENTERED AT 17:22:41 ON 19
     FEB 2003
L1         85846 "BACTERIA-TO-BACTERIA"
L2           384 L1 AND PLASMID AND GENES AND DNA
L3             7 L1 AND TAUROLIDINE
L4           202 L1(P)(PLASMID OR DNA)
L5            29 L4(P)(PREVENT? OR INHIBIT?)


=> "bacteria-to-bacteria"
L1        85846 "BACTERIA-TO-BACTERIA"

=> l1 and plasmid and genes and DNA
L2          384 L1 AND PLASMID AND GENES AND DNA

=> l1 and taurolidine
L3            7 L1 AND TAUROLIDINE

=> d l3 1-7 ibib ab

L3   ANSWER 1 OF 7  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER:   2002:558999  BIOSIS
DOCUMENT NUMBER:    PREV200200558999
TITLE:              Efficacy and tolerance of selected antiseptic substances
in
                    respect of suitability for use on the eye.
AUTHOR(S):          Kramer, A. (1); Rudolph, P.
CORPORATE SOURCE:   (1) Institute of Hygiene and Environmental Medicine, Ernst
                    Moritz Arndt University, Hainstrasse 26, D-17487,
                    Greifswald: kramer@uni-greifswald.de Germany
SOURCE:             Kramer, A. [Editor]; Behrens-Baumann, W. [Editor].
                    Developments in Ophthalmology, (2002) Vol. 33, pp.
117-144.
                    Developments in Ophthalmology. Antiseptic prophylaxis and
                    therapy in ocular infections: Principles, clinical
practice
                    and infection control. print.
                    Publisher: S. Karger AG CH-4009, Basel, Switzerland.
```

ISSN: 0250-3751. ISBN: 3-8055-7316-2 (cloth).
DOCUMENT TYPE: Book
LANGUAGE: English

L3 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:16921 BIOSIS
DOCUMENT NUMBER: PREV200000016921
TITLE: Local treatment of generalised peritonitis in rats; Effects on bacteria, endotoxin and mortality.
AUTHOR(S): Rosman, Camiel (1); Westerveld, Gert J.; Kooi, Kor; Bleichrodt, Robert P.
CORPORATE SOURCE: (1) Department of Surgery, University Hospital Groningen, NL-9700 RB, Groningen Netherlands
SOURCE: European Journal of Surgery, (Nov., 1999) Vol. 165, No. 11, pp. 1072-1079.
ISSN: 1102-4151.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: To assess the effect of debridement, intraoperative lavage with saline, and additional instillation of **taurolidine** or imipenem/cilastatin in rats with faecal peritonitis. Design: Laboratory study. Setting: University hospital, The Netherlands. Material: 60 male Wistar rats. Interventions: Rats were given an intraperitoneal injection of a faecal suspension containing Escherichia coli and Bacteroides fragilis. Six groups of 10: sham operation, debridement, debridement with saline lavage, debridement with saline lavage with intraperitoneal instillation of saline or **taurolidine**, or imipenem/cilastatin, were studied. Main outcome measures: Bacterial growth and endotoxin concentration in abdominal exudate and plasma, abscess formation, and mortality. Results: Debridement temporarily reduced bacterial growth and the concentration of endotoxin in abdominal exudate, and delayed mortality. Lavage with saline further reduced bacterial growth and the endotoxin concentration. It also reduced the plasma endotoxin concentration, and mortality. Additional instillation of **taurolidine** did not reduce bacterial growth, but did initially reduce the endotoxin concentration in abdominal exudate and plasma. Instillation of imipenem/cilastatin, after debridement and lavage, significantly reduced all variables measured. Conclusion: In rats with faecal peritonitis, debridement, lavage with saline, and additional instillation of imipenem/cilastatin, all have cumulatively reducing effect on bacterial growth, endotoxin concentrations, abscess formation, and mortality. Instillation of **taurolidine** reduces only the amount of endotoxin.

L3 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:402244 BIOSIS
DOCUMENT NUMBER: PREV199799708447
TITLE: Spectrum of pathogens and resistance in peritonitis.
AUTHOR(S): Focht, J. (1); Noesner, K.
CORPORATE SOURCE: (1) Biosci., Inst. Laboruntersuchungen, Zum Schuermannsgraben 30, D-47441 Moers Germany
SOURCE: Langenbecks Archiv fuer Chirurgie, (1997) Vol. 382, No. 4 SUPPL. 1, pp. S1-S4.
ISSN: 0023-8236.
DOCUMENT TYPE: Article

LANGUAGE: German
SUMMARY LANGUAGE: German; English
AB Severe intra-abdominal infection is associated with a high mortality rate.
In addition to risk factors in the patients, the causal pathogens and the selection of appropriate therapeutic procedures play an essential part in the course of these conditions. In the majority of intra-abdominal infections mixed aerobic/anaerobic infections, mostly with some involvement of enterobacteria and also of enterococci and staphylococci can be demonstrated. In addition to surgical intervention a calculated antimicrobial initial treatment of intra-abdominal infections with an antibiotic with an adequate effect to combat the pathogen concerned can contribute to improving the patient's prognosis. A calculated antibiotic treatment can only be effectively and reliably carried through if the frequency of the pathogen and the resistance situation are known. Retrospective evaluations of data on the sensitivity and frequency of pathogens from a defined group of subjects allow conclusions on the epidemiological situation in a particular catchment area or in a medical sector and thus make it possible to calculate the appropriate therapy for infections. In 1996 a total of 2,779 bacterial isolates from the intra-abdominal infection sector were examined: 935 Enterobacteriaceae, 83 nonfermenters, 177 Staphylococcus spp., 211 Enterococcus spp., 39 Streptococcus spp., and 1334 different anaerobic bacteria. Fresh clinical isolates were available for all pathogens tested. The most frequent gram-negative pathogen was E. coli (60%) and the most frequent gram-positive pathogen, E. faecalis (44%); the most frequent anaerobic pathogen was B. fragilis (39%). Taurolodine had the lowest resistance rate against gram-negative and anaerobic pathogens. Teicoplanin had the highest activity against gram-positive pathogens.

L3 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:510366 BIOSIS
DOCUMENT NUMBER: PREV199699232722
TITLE: Effect of intraperitoneal antimicrobials on the concentration of bacteria, endotoxin, and tumor necrosis factor in abdominal fluid and plasma in rats.
AUTHOR(S): Rosman, C. (1); Westerveld, G. J.; Van Oeveren, W.; Kooi, K.; Bleichrodt, R. P.
CORPORATE SOURCE: (1) Dep. Surgery, Medisch Spectrum Twente, PO Box 50.000, NL-7500 KA Enschede Netherlands
SOURCE: European Surgical Research, (1996) Vol. 28, No. 5, pp. 351-360.
ISSN: 0014-312X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The efficacy of intraperitoneal instillation of antimicrobial agents in eliminating the bacterial contaminant in patients with generalized peritonitis remains controversial. We determined the effect of intraperitoneal instillation of **taurolidine** or imipenem on mortality, and on the concentration of bacteria, eridotoxin, and tumor necrosis factor (TNF) in rats with intraperitoneally injected bacteria. Thirty rats were inoculated intraperitoneally with two enteric bacterial strains, followed by either **taurolidine**, saline, or imipenem. Abdominal fluid and blood were analyzed at different time intervals. The survival rate was highest in the imipenem group (p lt 0.05). The bacterial concentration in abdominal fluid in the **taurolidine** and imipenem

group was lower than in the saline group (p lt 0.005), but the concentration in the imipenem group was lowest (p lt 0.005). The endotoxin concentration in abdominal fluid and plasma in the **taurolidine** group was lower than in the other two groups (p lt 0.05). The TNF concentration in abdominal fluid and plasma in the **taurolidine** group was lower than in the saline group (p lt 0.05), whereas the concentration in the imipenem group was higher (p lt 0.005). We conclude that topically applied **taurolidine** in rats with intraperitoneally injected bacteria may have a weak antibacterial effect, and lowered concentrations of endotoxin and TNF. Topically applied imipenem had a profound bactericidal activity but induced endotoxin and TNF release.

L3 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:346923 BIOSIS
DOCUMENT NUMBER: PREV199598361223
TITLE: Effect of the antiendotoxic agent, **taurolidine**, in the treatment of sepsis syndrome: A placebo-controlled, double-blind trial.
AUTHOR(S): Willatts, Sheila M. (1); Radford, Sheila; Leitermann, Marie
CORPORATE SOURCE: (1) Intensive Therapy Unit, Bristol Royal Infirmary, Marlborough Street, Bristol BS2 8HW UK
SOURCE: Critical Care Medicine, (1995) Vol. 23, No. 6, pp. 1033-1039.
ISSN: 0090-3493.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Objective: To assess the benefit gained from administration of the antiendotoxic drug, **taurolidine**, on outcome in critically ill patients with sepsis syndrome. Design: A prospective, randomized, double-blind trial. Setting. The general intensive therapy unit in a university teaching hospital. Patients: One hundred patients admitted with sepsis syndrome over a 2-yr period. Interventions: Patients were randomized to receive the amino-acid derivative, **taurolidine**, or an identically presented placebo. Measurements and Main Results: Acute Physiology and Chronic Health Evaluation II (APACHE II), sepsis, and organ failure scores were measured daily. Blood for culture and endotoxin assay (using the limulus amoebocyte lysate assay) was sampled every 12 hrs for up to 5 days. Hemodynamic variables were recorded every 4 hrs. Forty-nine patients received **taurolidine** and 51 patients received placebo. There was no difference in APACHE II score, Sepsis Score, or presence of infections between the groups. The frequency of Gram-negative bacteremia was low at 12%. There was no difference in endotoxin activity, clinical or bacteriologic outcome, resolution of organ failure, or mortality rate between groups. Predicted risk of death for patients receiving **taurolidine** was 45%, and the actual mortality rate was 44%. In the group that received placebo, the predicted mortality rate was 38% and the actual mortality rate was 39%. Conclusion: **Taurolidine** had no beneficial therapeutic effect on the outcome of patients admitted to the intensive therapy unit with sepsis syndrome, using clinical, bacteriologic outcomes, progression of endotoxemia, resolution of organ failure, and 28-day mortality rate as end points.

L3 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1994:13881 BIOSIS
DOCUMENT NUMBER: PREV199497026881
TITLE: **Taurolidine**, anti-lipopolysaccharide (LPS) agent with immunostimulatory properties.
AUTHOR(S): Watson, R. William G. (1); Redmond, H. Paul; McCarthy, Julie; Croke, T. David; Burke, Paul; Bouchier-Hayes, David
CORPORATE SOURCE: (1) Dep. Surg., Beaumont Hosp., Dublin Ireland
SOURCE: Surgical Forum, (1993) Vol. 44, No. 0, pp. 90-91.
ISSN: 0071-8041.
DOCUMENT TYPE: Article
LANGUAGE: English

L3 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:25354 BIOSIS
DOCUMENT NUMBER: PREV199395013554
TITLE: In vitro activity of **taurolidine**, chlorophenol-camphor-menthol and chlorhexidine against oral pathogenic microorganisms.
AUTHOR(S): Zimmermann, M. (1); Preac-Mursic, V.
CORPORATE SOURCE: (1) Klin. Poliklin. Kieferchirurgie, Univ. Munechen, Lindwurmstr. 2a, W-8000 Muenchen 2 Germany
SOURCE: Arzneimittel-Forschung, (1992) Vol. 42, No. 9, pp. 1157-1159.
ISSN: 0004-4172.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English; German
AB The antimicrobial activity of **taurolidine** (Taurolin, CAS 19388-87-5), a synthetic broad-spectrum antimicrobial agent and anti-toxin, and two conventional antiseptics, chlorophenol-camphor-menthol (CCM) and chlorhexidine digluconate (CHX) were compared using the serial dilution test on 10 potential oral pathogenic bacterial species. The minimum inhibitory and minimum bactericidal concentrations were lowest for CHX (MIC 0.03-0.12 mg/ml), followed by **taurolidine** (MIC 0.12-0.5 mg/ml) and CCM (MIC 0.5-2.0 mg/ml). However, if both bacterial efficacy and cytotoxicity are considered, only **taurolidine** achieves extensive bactericidal activity with tissue tolerability.

=> d his

(FILE 'HOME' ENTERED AT 17:22:04 ON 19 FEB 2003)

FILE 'CAPLUS, WPIDS, BIOSIS, MEDLINE, EMBASE' ENTERED AT 17:22:41 ON 19 FEB 2003
L1 85846 "BACTERIA-TO-BACTERIA"
L2 384 L1 AND PLASMID AND GENES AND DNA
L3 7 L1 AND TAUROLIDINE

=> l1(p)(plasmid or DNA)
L4 202 L1(P)(PLASMID OR DNA)

=> l4(p)(prevent? or inhibit?)
L5 29 L4(P)(PREVENT? OR INHIBIT?)

=> d l5 1-29 ibib ab

L5 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:740747 CAPLUS
DOCUMENT NUMBER: 138:12965
TITLE: Review article: the role of the gut flora in health and disease, and its modification as therapy
AUTHOR(S): Hart, A. L.; Stagg, A. J.; Frame, M.; Graffner, H.; Glise, H.; Falk, P.; Kamm, M. A.
CORPORATE SOURCE: St Mark's Hospital, Harrow, Middlesex, UK
SOURCE: Alimentary Pharmacology and Therapeutics (2002), 16(8), 1383-1393
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The gut flora is a vast interior ecosystem whose nature is only beginning to be unravelled, due to the emergence of sophisticated mol. tools. Techniques such as 16S rRNA anal., polymerase chain reaction amplification and the use of **DNA** microarrays now facilitate rapid identification and characterization of species resistant to conventional culture and possibly unknown species. Life-long cross-talk between the host and the gut flora dets. whether health is maintained or disease intervenes. An understanding of these **bacteria**-**bacteria** and **bacteria**-host immune and epithelial cell interactions is likely to lead to a greater insight into disease pathogenesis. Studies of single organism-epithelial interactions have revealed the large range of metabolic processes that gut bacteria may influence. In inflammatory bowel diseases, bacteria drive the inflammatory process, and genetic predisposition to disease identified to date, such as the recently described NOD2/CARD15 gene variants may relate to altered bacterial recognition. Extra-intestinal disorders, such as atopy and arthritis, may also have an altered gut milieu as their basis. Clin. evidence is emerging that the modification of this internal environment, using either antibiotics or probiotic bacteria, is beneficial in **preventing** and treating disease. This natural and apparently safe approach holds great appeal.
REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:90224 CAPLUS
DOCUMENT NUMBER: 136:129913
TITLE: Mutational analysis in isolation of regulated virulence determinants of bacterial pathogens and the rtxA and enhC genes from Legionella pneumophila
INVENTOR(S): Cirillo, Jeffrey D.
PATENT ASSIGNEE(S): The Board of Regents of the University of Nebraska, USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002008418 A2 20020131 WO 2001-US23306 20010724
WO 2002008418 A3 20020613
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-628871 A 20000724

AB The present invention relates to novel methods for isolation and identification of virulence determinants from bacterial pathogens. The present invention also relates to novel genes of the Legionella pneumophila bacteria, and methods of detection of Legionella pneumophila bacteria in samples. The present invention relates to novel methods for isolation and identification of virulence determinants from bacterial pathogens. A pool of bacterial mutants with enhanced virulence phenotype is obtained, and the **DNA** responsible as a factor for the enhanced virulence is located. Random mutations are inserted into the **DNA**, the **DNA** transferred into wild-type **bacteria**, and **bacteria** that no longer express the enhanced virulence are selected in order to identify an active site of the **DNA** necessary to confer enhanced virulence. The present invention also more specifically relates to novel rtxA and enhC genes of the Legionella pneumophila bacteria. Gene rtxA affects bacterial adherence to monocytes and epithelial cells, is involved in cytotoxicity and pore formation by L. pneumophila, and affects the bacterial virulence. These genes allow for the detection and quantitation of L. pneumophila and thus diagnosis of Legionnaires' disease, as well as for the design of **inhibitors** of the protein products of the genes.

L5 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:12666 CAPLUS
DOCUMENT NUMBER: 134:96206
TITLE: General method for isolation of regulated virulence determinants from bacterial pathogens and the rtxA and enhC genes from Legionella pneumophila
INVENTOR(S): Cirillo, Jeffrey D.
PATENT ASSIGNEE(S): The Board of Regents of the University of Nebraska, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000877	A2	20010104	WO 2000-US17743	20000627
WO 2001000877	A3	20020510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,

ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002086304	A1	20020704	US 2001-881901	20010615
US 2002086981	A1	20020704	US 2001-882583	20010615
PRIORITY APPLN. INFO.:			US 1999-141717P	P 19990630
			US 2000-604561	A3 20000627

AB The present invention relates to novel methods for isolation and identification of virulence determinants from bacterial pathogens. A pool of bacterial mutants with enhanced virulence phenotype is obtained, and the **DNA** responsible as a factor for the enhanced virulence is located. Random mutations are inserted into the **DNA**, the **DNA** transferred into wild-type **bacteria**, and **bacteria** that no longer express the enhanced virulence are selected in order to identify an active site of the **DNA** necessary to confer enhanced virulence. The present invention also more specifically relates to novel rtxA and enhC genes of the Legionella pneumophila bacteria. Gene rtxA affects bacterial adherence to monocytes and epithelial cells, is involved in cytotoxicity and pore formation by L. pneumophila, and affects the bacterial virulence. These genes allow for the detection and quantitation of L. pneumophila and thus diagnosis of Legionnaires' disease, as well as for the design of **inhibitors** of the protein products of the genes.

L5 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1996:261712 CAPLUS
DOCUMENT NUMBER:	124:308780
TITLE:	Update on gene amplification kits for medical bacteriological laboratory
AUTHOR(S):	Stoessel, P.; Jaulhac, B.
CORPORATE SOURCE:	Faculte de Medecine, Institut de Bacteriologie de la, Strasbourg, 67000, Fr.
SOURCE:	Spectra Biologie (1996), 15(76), 37-42 CODEN: SPEBEQ; ISSN: 0295-1967
PUBLISHER:	Spectra Biologie
DOCUMENT TYPE:	Journal
LANGUAGE:	French

AB Recent developments in mol. biol. allow detection of fastidious **bacteria** or **bacteria** requiring a long culture time. Two methods exist, **DNA** hybridization and nucleic acid amplification. **DNA** hybridization is specific and rapid but is not sensitive enough to be used with low inoculums. However, with the amplification techniques, the sensitivity is increased. The purpose of the present article is to evaluate the nucleic acid amplification tests which are com. available in 1995 or will be available. Two types of tests exist: non-isothermic tests using polymerase chain reaction or ligase chain reaction requiring a thermocycler to automate thermal variation, and isothermic tests (transcription mediated amplification, nucleic acid based amplification, strand displacement amplification) which only require an incubator. Kits currently available for bacteriol. applications are for Chlamydia trachomatis and mycobacteria. These kits have a sensitivity of greater than 90% and a specificity approaching 100%. However, there are tech. limitations for these methods such as the **inhibitors** of enzyme activity (leading to false neg. results) and contamination (leading

to false pos. results).

L5 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:135100 CAPLUS
DOCUMENT NUMBER: 106:135100
TITLE: Antibacterial activity and mechanism of action of 3'-azido-3'-deoxythymidine (BW A509U)
AUTHOR(S): Elwell, Lynn P.; Ferone, Robert; Freeman, G. Andrew; Fyfe, James A.; Hill, John A.; Ray, Paul H.; Richards, Cynthia A.; Singer, Sara C.; Knick, Victoria B.; et al.
CORPORATE SOURCE: Dep. Microbiol., Wellcome Res. Lab., Research Triangle Park, NC, 27709, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1987), 31(2), 274-80
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The thymidine analog 3'-azido-3'-deoxythymidine (AZT) had potent bactericidal activity against many members of the family Enterobacteriaceae, including strains of Escherichia coli, Salmonella typhimurium, Klebsiella pneumoniae, Shigella flexneri, and Enterobacter aerogenes. AZT also had bactericidal activity against Vibrio cholerae and the fish pathogen V. anguillarum. AZT had no activity against Pseudomonas aeruginosa, gram-pos. **bacteria**, anaerobic **bacteria**, Mycobacterium tuberculosis, nontuberculosis mycobacteria, or most fungal pathogens. Several lines of evidence indicated that AZT must be activated to the nucleotide level to **inhibit** cellular metab.: (1) AZT was a substrate for E. coli thymidine kinase, (2) spontaneously arising AZT-resistant mutants of E. coli ML-30 and S. typhimurium were deficient in thymidine kinase, and (3) intact E. coli ML-30 cells converted [3H]AZT to its mono-, di-, and triphosphate metabolites. Of the phosphorylated metabolites, AZT-5'-triphosphate was the most potent **inhibitor** of replicative **DNA** synthesis in toluene-permeabolized E. coli pol A mutant cells. AZT-treated E. coli cultures grown in minimal medium contained highly elongated cells consistent with the **inhibition** of **DNA** synthesis. AZT-triphosphate was a specific **DNA** chain terminator in the in vitro **DNA** polymn. reaction catalyzed by the Klenow fragment of E. coli **DNA** polymerase I. Thus, **DNA** chain termination may explain the lethal properties of this compd. against susceptible microorganisms.

L5 ANSWER 6 OF 29 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-590500 [63] WPIDS
DOC. NO. CPI: C2002-166963
TITLE: New DNA methyltransferase inhibitors useful in the treatment of bacterial infections e.g. bacterial meningitis.
DERWENT CLASS: B03
INVENTOR(S): BABOVAL, J; BAKER, S J; BENKOVIC, S J; SCOTT, C P; SHAPIRO, L; SHIER, V K; WAHNON, D C; WALL, M
PATENT ASSIGNEE(S): (PENN-N) PENN STATE RES FOUND
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002044184	A2	20020606	(200263)*	EN	35

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002039407 A 20020611 (200264)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002044184	A2	WO 2001-US45129	20011129
AU 2002039407	A	AU 2002-39407	20011129

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002039407	A	Based on	WO 200244184

PRIORITY APPLN. INFO: US 2000-250202P 20001130

AB WO 200244184 A UPAB: 20021031

NOVELTY - DNA methyltransferase inhibitors (I) are new.

DETAILED DESCRIPTION - DNA methyltransferase inhibitors of formula (I) and their salts are new.

A = N, O or S;

W = Cp;

p = 0-1;

Ra-Re = cycloalkyl, cycloalkyl alkoxy (where the cycloalkyl group has 3-7 members and up to 2 atoms are optionally substituted by heteroatoms selected from S, O or N), lower alkyl, optionally substituted aryl (all optionally substituted by halo, lower alkyl, lower alkoxy, optionally substituted aryl, nitro, nitroso, aldehyde, carboxylic acid, amide, ester or sulfate), H, halo, nitro, nitroso, lower alkoxy or lower alkoxyalkyl; and

Ra-Re = connected by optionally substituted aromatic, aliphatic, heteroaromatic, heteroaliphatic rings;

Ar1, Ar2 = optionally substituted aryl (substituted by at least one position by Ra);

Ar1+Ar2 = tricyclic scaffold of formula (i);

X = C=O, CHOH, (CH2)n, CH=CH, NRf, O, SOn (having several positions with cycloalkyl, cycloalkyl alkoxy (in which cycloalkyl has 3-7 members and in which up to two cycloalkyl members are optionally heteroatoms selected from S, O or N), halo, nitro, nitroso, lower alkyl, optionally substituted aryl, lower alkoxy or lower alkoxyalkyl; and

a'-d' = single or double bond;

provided that:

(i) when A is O or S, Ra is absent;

(ii) when p is 0, Rd is absent; and

(iii) when A is S or O, a' is single bond and when A is N, a' is a double bond.

INDEPENDENT CLAIMS are also included for:

(1) a combinatorial library comprising multiplicity of (I); and

(2) a packaged pharmaceutical composition comprising the composition in a container and instructions for using the composition in the treatment

of a patient suffering from a disease associated with infection with a pathogenic bacterium.

ACTIVITY - Antibacterial; Antiinflammatory; Immunosuppressive; Antirheumatic; Antipyretic.

MECHANISM OF ACTION - DNA methyltransferase inhibitor; Cellular process modulator; Cell growth inhibitor.

In a cell growth assay using Bacillus subtilis, di-(para-chlorophenyl)borinic acid 8-hydroxyquinaldine ester (Ia) inhibited cell growth with an IC50 of 24 micro M.

USE - In the treatment of disease associated with infection with pathogenic bacteria such as Staphylococcus aureus, Staphylococcus saprophyticus, Streptococcus pyrogenes, Streptococcus agalactiae, Streptococcus pneumoniae, Bacillus anthracis, Corynebacterium diphtheria, Clostridium perfringens, Clostridium botulinum, Clostridium tetani, Neisseria gonorrhoeae, Neisseria meningitidis, Pseudomonas aeruginosa, Legionella pneumophila, Escherichia coli, Yersinia pestis, Hemophilus influenzae, Helicobacter pylori, Campylobacter fetus, Vibrio cholerae, Vibrio parahemolyticus, Trepomena pallidum, Actinomyces israelii, Rickettsia prowazekii, Rickettsia rickettsii, Chlamydia trachomatis, Chlamydia psittaci, Brucella abortus and Agrobacterium tumefaciens expressing adenine DNA methyltransferase (all claimed). As antibiotic in the treatment of actinomycosis, anthrax, bacterial dysentery, botulism, brucellosis, cellulitis, cholera, conjunctivitis, cystitis, diphtheria, bacterial endocarditis, epiglottitis, gastroenteritis, glanders, gonorrhea, Legionnaire's disease, leptospirosis, bacterial meningitis, palgue, bacterial pneumonia, puerperal sepsis, rheumatic fever, Rocky Mountain spotted fever, scarlet fever, streptococcal pharyngitis, syphilis, tetanus, tularemia, typhoid fever, typhus and pertussis.

ADVANTAGE - (I) Exhibits DNA methyltransferase inhibitory activity. (I) Exhibits low cytosine-specific DNA methyltransferase activity. (I) Is bacterial cell specific and has little antibiotic activity against mammalian.

Dwg.0/0

L5 ANSWER 7 OF 29 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 2002-557291 [59] WPIDS

CROSS REFERENCE: 2000-532863 [48]; 2002-598710 [64]; 2002-635659 [68]; 2002-635674 [68]; 2002-690113 [74]

DOC. NO. CPI: C2002-158052

TITLE: Reducing bacterial virulence using an agent that alters the bacteria's native level of DNA methyltransferase activity.

DERWENT CLASS: B04 D16

INVENTOR(S): HEITHOFF, D M; LOW, D A; MAHAN, M J; SINSHEIMER, R L

PATENT ASSIGNEE(S): (HEIT-I) HEITHOFF D M; (LOWD-I) LOW D A; (MAHA-I) MAHAN M J; (SINS-I) SINSHEIMER R L

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002077272	A1	20020620	(200259)*		35

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002077272 A1	Provisional	US 1999-183043P	19990202
	Provisional	US 1999-198250P	19990505

CIP of	US 2000-495614	20000201
CIP of	US 2000-612116	20000707
	US 2001-927885	20010809

PRIORITY APPLN. INFO: US 2001-927885 20010809; US 1999-183043P 19990202; US 1999-198250P 19990505; US 2000-495614 20000201; US 2000-612116 20000707

AB US2002077272 A UPAB: 20021120

NOVELTY - Reducing bacterial virulence comprising contacting bacteria with an agent that alters the bacteria's native level of **DNA** methyltransferase (Dam) activity thereby altering the bacteria's native level of methylation of adenine in a GATC tetranucleotide of the bacteria, and thereby **inhibiting** virulence of the bacteria.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) reducing pathogenicity of a pathogenic bacteria, comprising administering an agent that alters a pathogenic bacteria's native Dam activity thereby altering the bacteria's native **DNA** methylation activity to an extent that the bacteria's pathogenicity is reduced;

(2) treating a bacterial infection, comprising administering to a subject infected with a pathogenic bacteria a therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and an agent that alters the bacteria's native level of Dam activity;

(3) treating bacterial infection comprising administering an agent that reduces the level or activity of a **DNA** methyltransferase thus reducing methylation of adenine in a GATC tetranucleotide in the bacteria, **inhibiting** the virulence of the bacteria;

(4) a composition for controlling bacterial pathogenicity, comprising a carrier, and a compound that alters native Dam activity; and

(5) an attenuated strain of a **bacteria**, the **bacteria** comprising altered Dam activity.

ACTIVITY - Antibacterial. No suitable biodata provided.

MECHANISM OF ACTION - **DNA** methyltransferase activity modulator.

USE - The methods are useful for reducing bacterial virulence; reducing pathogenicity of a pathogenic bacteria, comprising administering an agent that alters a pathogenic bacteria's native Dam activity thereby altering the bacteria's native **DNA** methylation activity to an extent that the bacteria's pathogenicity is reduced; and treating a bacterial infection, the bacteria are e.g. Haemophilus, salmonella, Escherichia, and Vibrio (claimed).

Dwg.0/9

L5 ANSWER 8 OF 29 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER:	2001-292928 [31] WPIDS
DOC. NO. CPI:	C2001-089883
TITLE:	New enolase gene from coryneform bacteria, used to prepare transformants with increased synthesis of amino acids, particularly lysine.
DERWENT CLASS:	B05 D16 E16
INVENTOR(S):	BATHE, B; HERMANN, T; KALINOWSKI, J; MOCKEL, B; PFEFFERLE, W; PUHLER, A; MOECKEL, B; PUEHLER, A
PATENT ASSIGNEE(S):	(DEGS) DEGUSSA-HUELS AG; (BATH-I) BATHE B; (HERM-I) HERMANN T; (KALI-I) KALINOWSKI J; (MOCK-I) MOCKEL B; (PFEF-I) PFEFFERLE W; (PUHL-I) PUHLER A
COUNTRY COUNT:	35

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1090998	A1	20010411	(200131)*	GE	25
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
DE 19947791	A1	20010412	(200131)		
AU 2000061359	A	20010412	(200132)		
CA 2319716	A1	20010405	(200133)	EN	
BR 2000004643	A	20010612	(200137)		
CN 1290750	A	20010411	(200140)		
JP 2001161380	A	20010619	(200140)		13
ZA 2000005409	A	20010627	(200140)		34
SK 2000001458	A3	20010710	(200157)		
KR 2001050840	A	20010625	(200172)		
US 2002082403	A1	20020627	(200245)		
HU 2000003893	A1	20020930	(200272)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 1090998	A1		EP 2000-121158	20000929
DE 19947791	A1		DE 1999-19947791	19991005
AU 2000061359	A		AU 2000-61359	20000928
CA 2319716	A1		CA 2000-2319716	20001004
BR 2000004643	A		BR 2000-4643	20001004
CN 1290750	A		CN 2000-129571	20000927
JP 2001161380	A		JP 2000-305110	20001004
ZA 2000005409	A		ZA 2000-5409	20001004
SK 2000001458	A3		SK 2000-1458	20000929
KR 2001050840	A		KR 2000-58213	20001004
US 2002082403	A1	CIP of	US 1999-455779	19991207
			US 2001-860768	20010521
HU 2000003893	A1		HU 2000-3893	20001004

PRIORITY APPLN. INFO: DE 1999-19947791 19991005

AB EP 1090998 A UPAB: 20010615

NOVELTY - An isolated nucleic acid (I) from coryneform bacteria encoding a polypeptide at least 70 % identical with a 425 residue amino acid sequence (S2), or having a complementary nucleotide sequence, or at least 15 consecutive bases of it, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for fermentative production of L-amino acids, especially L-lysine, by fermenting a lysine-producing coryneform in which the eno gene has been amplified, and isolating amino acids that have accumulated in the medium or cells.

USE - (I), which encodes an enolase, is used to transform coryneforms for production of L-amino acids, specifically lysine which is used in medicine and particularly as animal feed supplement (claimed). It may also be used as probes and primers for isolating related sequences.

ADVANTAGE - Overexpression of (I) improves production of amino acids, especially of L-lysine.

Dwg.0/2

L5 ANSWER 9 OF 29 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-202774 [20] WPIDS
DOC. NO. NON-CPI: N2001-144679
DOC. NO. CPI: C2001-060211
TITLE: Enzymes which operate in the alternative isoprenoid pathway downstream from 2C-methyl-D-erythritol-4-phosphate, useful for screening a chemical library for inhibitors of the biosynthesis of isoprenoids.
DERWENT CLASS: C06 D16 S03
INVENTOR(S): BACHER, A; EISENREICH, W; FELLERMEIER, M; FISCHER, M; HECHT, S; HERZ, S; KIS, K; LUETTGEN, H; ROHDICH, F; SAGNER, S; SCHUHR, C A; WUNGSINTAWEEKUL, J; ZENK, M
PATENT ASSIGNEE(S): (BACH-I) BACHER A; (ZENK-I) ZENK M; (ZENK-I) ZENK M H
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001011055	A1	20010215	(200120)*	EN	180
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
DE 10020996	A1	20010322	(200124)		
AU 2000062803	A	20010305	(200130)		
EP 1198575	A1	20020424	(200235)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001011055	A1	WO 2000-EP7548	20000803
DE 10020996	A1	DE 2000-10020996	20000428
AU 2000062803	A	AU 2000-62803	20000803
EP 1198575	A1	EP 2000-949452	20000803
		WO 2000-EP7548	20000803

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000062803	A	Based on	WO 200111055
EP 1198575	A1	Based on	WO 200111055

PRIORITY APPLN. INFO: DE 2000-10020996 20000428; DE 1999-19936663 19990804; DE 1999-19945174 19990921; DE 1999-19945175 19990921; DE 1999-19948887 19991011; DE 1999-19953309 19991105

AB WO 200111055 A UPAB: 20010410
NOVELTY - Functional enzymes which operate in the alternative isoprenoid pathway downstream from 2C-methyl-D-erythritol-4-phosphate, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for the following:
(1) a protein (P1), in a form that is enzymatically functional for

the conversion of cytidine triphosphate and 2C-methyl-D-erythritol-4-phosphate into 4-diphosphocytidyl-2C-methyl-D-erythritol in the presence of magnesium ions;

(2) a protein (P2), in a form that is enzymatically functional for the conversion of 4-diphosphocytidyl-2C-methyl-D-erythritol in the presence of manganese ions;

(3) a protein (P3), in a form that is enzymatically functional for the conversion of 4-diphosphocytidyl-2C-methyl-D-erythritol and adenosine triphosphate (ATP) into 4-diphosphocytidyl-2C-methyl-D-erythrtol-2-phosphate in the presence of a magnesium salt;

(4) a protein (P4), in a form that is enzymatically functional for the conversion of 4-diphosphocytidyl-2C-methyl-D-erythrtol-2-phosphate into 2C-methyl-D-erythrtol-2,4-cyclopyrophosphate and cytidine monophosphate (CMP);

(5) a protein (P5) in a form that is enzymatically bifunctional, having an N-terminal domain with the function of synthesis of diphosphocytidyl-2C-methyl-D-erythritol from cytidine triphosphate and 2C-methyl-D-erythritol-4-phosphate and a C-terminal domain with the function of the conversion of 4-diphosphocytidyl-2C-methyl-D-erythritol or

the function of the conversion of 4-diphosphocytidyl-2-C-methyl-D-erythritol-2-phosphate into 2C-methyl-D-erythritol-2, 4-cyclopyrophosphate and CMP;

(6) purified isolated nucleic acid (N1) encoding P1, P2, P3, P4 or P5 and optionally comprising introns;

(7) a **DNA** expression vector comprising N1;

(8) a cell comprising the vector of (7), where the cell is selected from a bacterial, protozoal, fungal, plant, insect or mammalian cell;

(9) a seed comprising a plant cell as defined in (8);

(10) a method (M1) for screening chemical libraries for the presence or absence of **inhibition** of the biosynthesis of isoprenoids by blocking the synthesis of 4-diphosphocytidyl-2C-methyl-D-erythritol from cytidine triphosphate (CTP) and 2C-methyl-D-erythritol-4-phosphate, comprising:

(a) preparing an aqueous mixture comprising P1, 2C-methyl-D-erythritol-4-phosphate or its source, CTP and a divalent metal salt;

(b) reacting the mixture for a predetermined period of time at a predetermined temperature;

(c) detecting the level of conversion to 4-diphosphocytidyl-2C-methyl-D-erythritol;

(d) repeating steps (a) to (c) in the presence of a test sample of a chemical library;

(e) determining the presence or absence of **inhibition** in step (d) by ascertaining whether or not the detected level is lower in the presence of the test sample;

(11) a method (M2) for screening chemical libraries for the presence or absence of **inhibition** of the biosynthesis of isoprenoids by blocking the conversion of 4-diphosphocytidyl-2C-methyl-D-erythritol;

(12) a method (M3) for screening chemical libraries for the presence or absence of **inhibition** of the biosynthesis of isoprenoids by blocking the synthesis of 4-diphosphocytidyl-2C-methyl-D-erythritol-2-phosphate from 4-diphosphocytidyl-2C-methyl-D-erythritol and ATP;

(13) a method (M4) for screening chemical libraries for the presence or absence of **inhibition** of the biosynthesis of isoprenoids by blocking the biosynthesis of isoprenoids by blocking the synthesis of 2C-methyl-D-erythritol-2 ,4-cyclopyrophosphate;

(14) Isotope labelled 4-diphosphocytidyl-2 C-methyl-D-erythritol, 2C-methyl-D-erythritol-3,4-cyclophosphate, 4-diphosphocytidyl-2C-methyl-D-erythritol-2-phosphate and 2C-methyl-D-erythritol-2, 4-cyclopyrophosphate, or their salts;

(15) a process for forming 4-diphosphocytidyl-2C-methyl-D-erythritol or its salt by reacting CTP and 2C-methyl-D-erythritol-4-phosphate in the presence of P1 and a divalent metal salt;

(16) a process for forming 2C-methyl-D-erythritol-3,4-cyclophosphate or its salt by reacting 4-diphosphocytidine-2C-methyl-D-erythritol in the presence of P2 and a divalent metal salt;

(17) a process for forming 4-diphosphocytidyl-2C-methyl-D-erythritol-2-phosphate or its salt by reacting 4-diphosphocytidyl-2C-methyl-D-erythritol with ATP in the presence of P3 and a divalent metal salt;

(18) a process for forming 2C-methyl-D-erythritol-2,4-cyclopyrophosphate or its salt by reacting 4-diphosphocytidyl-2C-methyl-D-erythritol-2-phosphate with P4;

(19) a method (M5) for identifying **inhibitor**-resistant variants of P1-P4;

(20) a variant protein (P6) of P1-P5, where the protein is herbicide resistant;

(21) a nucleic acid (N2) encoding P6;

(22) a **DNA** vector comprising N2;

(23) a cell comprising the vector of (22), where the cell is selected from a bacterial, protozoal, fungal, plant, insect or mammalian cell;

(24) a seed comprising a plant cell as defined in (23);

(25) a method for conferring herbicide-resistance in a plant, comprising introducing N2 under conditions in which the nucleic acid is expressed in the plant;

(26) a method for weed control comprising cultivating a crop containing herbicide-resistant gene having the sequence of N2 in the presence of a weed-controlling effective amount of the herbicide;

(27) Inhibitor for the biosynthesis of isoprenoids selected from chemical compounds which show enzyme inhibition in accordance with the screening methods of M1-M4;

(28) a method for the inhibition of the biosynthesis of isoprenoids in plants, bacteria or protozoa by treatment with an inhibitor of (27); and

(29) a comprehensive process (M6) for preparing intermediates in the isoprenoid pathway downstream from 2C-methyl-D-erythritol 4-phosphate.

ACTIVITY - None given.

No biological data given.

MECHANISM OF ACTION - Isoprenoid biosynthesis inhibitor.

No biological data given.

USE - The enzymes are useful for screening a chemical library for inhibitors of the biosynthesis of isoprenoids. 4-diphosphocytidyl-2C-methyl-D-erythritol, 2C-methyl-D-erythritol-2,4-cyclopyrophosphate or 4-diphosphocytidyl-2C-methyl-D-erythritol-2-phosphate, or their salts are useful for screening for inhibitors of the biosynthesis of isoprenoids.

Herbicide resistant enzymes can be used as genetic markers in any cell that is normally sensitive to the inhibitory effects of herbicide formation. The methods can be used to produce herbicide resistant enzyme variants which can be incorporated into plants to confer selective herbicide resistant on the plants. The methods are also useful for controlling weed by cultivating crops containing herbicide-resistant genes

in the presence of weed-controlling effective amounts of herbicides.
The inhibitors are used for inhibiting the biosynthesis of isoprenoids in plants, bacteria or protozoa.
Dwg.0/3

L5 ANSWER 10 OF 29 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-350764 [30] WPIDS
DOC. NO. CPI: C2000-106790
TITLE: Characterizing drug-target interactions and identifying genetic mutations that confer resistance to antibacterial compounds.
DERWENT CLASS: B02 B04 C06 D16
INVENTOR(S): DUNHAM, S A; OLSON, E
PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO
COUNTRY COUNT: 81
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000024932	A1	20000504	(200030)*	EN	49
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AU BA BB BG BR CA CN CR CU CZ DM EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT TZ UA US UZ VN YU ZA					
AU 9961607	A	20000515	(200039)		
BR 9914844	A	20010710	(200142)		
EP 1124988	A1	20010822	(200149)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002528094	W	20020903	(200273)		56
MX 2001003289	A1	20011001	(200274)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000024932	A1	WO 1999-US22118	19990923
AU 9961607	A	AU 1999-61607	19990923
BR 9914844	A	BR 1999-14844	19990923
		WO 1999-US22118	19990923
EP 1124988	A1	EP 1999-948428	19990923
		WO 1999-US22118	19990923
JP 2002528094	W	WO 1999-US22118	19990923
		JP 2000-578484	19990923
MX 2001003289	A1	MX 2001-3289	20010329

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9961607	A	Based on	WO 200024932
BR 9914844	A	Based on	WO 200024932
EP 1124988	A1	Based on	WO 200024932
JP 2002528094	W	Based on	WO 200024932

PRIORITY APPLN. INFO: US 1998-105965P 19981028
AB WO 200024932 A UPAB: 20000624
NOVELTY - Methods for identifying and characterizing mutations within

bacterial **DNA** gyrase and FabI that confer resistance to antibacterial compounds, are new. The methods combine random mutagenesis of genes coding for known targets of antibacterial compounds with homologous recombination to identify point mutations resulting in resistance.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a process (I) for identifying and characterizing mutations leading to a selectable phenotype comprising:

(a) generating a defined set of overlapping 10 kilobase (kb) polymerase chain reaction (PCR) products containing random point mutations which encompass the complete chromosome of an organism;

(b) transforming pools of 12 PCR product corresponding to 100 kb of the chromosome into a wild-type background;

(c) isolating strains of bacteria resistant to compound;

(d) re-transforming sensitive bacteria with individual products (10 kb) from resistant strains to identify a region with 1 or more mutations;

(e) generating smaller PCR products (1 kb) to further map mutation(s) responsible for phenotype; and

(f) sequencing **DNA** from a region conferring resistance to identify the chromosomal mutation;

(2) a process (II) for identifying and characterizing quinolone-**DNA** gyrase interactions using Neisseria gonorrhoeae (GC) comprising:

(a) mutagenizing randomly the quinolone resistance determining region (QRDR) of gyrA using oligonucleotide mediated site-specific mutagenesis with a degenerate oligonucleotide or mutagenizing the entire gene using low-fidelity PCR;

(b) transforming these random mutations into a wild-type back-ground;

(c) selecting isogenic quinolone resistant mutations following homologous recombination;

(d) sequencing the gyrA QRDR confirming that Ser91 and ASp95 are independently involved in quinolone **inhibition** of **DNA** gyrase;

(e) identifying the following mutation associated with quinolone resistance in N. gonorrhoeae: Asp90 to Glu, Ser91 to Cys, Asp95 to His, Glu161 to Gly, Glu161 to Lys, Asn 65 to His, Asp80 to Gly and/or Glu62 to Lys; and

(f) using these mutants to help to understand the mechanism of action of quinolones and other type IV **inhibitors**;

(3) mutations in N. gonorrhoeae GyrA associated with quinolone resistance selected from: Asp90 to Glu, Ser91 to Cys, Asp95 to His, Glu161 to Gly, Glu161 to Lys, Asn 65 to His, Asp80 to Gly and/or Glu62 to Lys;

(4) a process (III) for identifying and characterizing a mechanism of action of an antibacterial compound comprising:

(a) generating **DNA** fragments by PCR amplification of **DNA** from bacteria under conditions that allow for mutations of the fragments;

(b) allowing 1 or more of the generated **DNA** fragments to be incorporated into the chromosome of a bacteria by homologous recombination;

(c) isolating the bacteria that demonstrate resistance to an antibacterial compound; and

(d) identifying the mutation contained in the **DNA** fragment;

(5) a process (IV) for identifying mutations contained in the chromosome of a bacteria that results in an identifiable phenotype comprising:

(a) generating **DNA** fragments by PCR amplification of the bacterial chromosome corresponding to regions of the bacterial chromosome which may contain a mutation;

(b) allowing 1 or more of the **DNA** fragments to be incorporated into the chromosome of a bacteria that does not display the identifiable phenotype by homologous recombination;

(c) isolating bacteria that demonstrate the identifiable phenotype;

(d) repeating steps (a) to (c) until a single **DNA** fragment less than 10 kb in length is identified as being responsible for the phenotype; and

(e) identifying the mutation contained in the **DNA** fragments;

(6) bacteria (V) comprising a protein in which a contiguous stretch of 40 amino acids is at least 30% identical to residues 75-114 of the N. gonorrhoeae GyrA and the residue analogous to:

(a) 62 is Lys;

(b) 63 is Arg or Glu;

(c) 65 is His;

(d) 135 is Val; or

(e) 161 is Glu, Lys or Arg;

(7) a protein (VI) comprising a contiguous stretch of 40 amino acids is at least 30% identical to residues 75-114 of the N. gonorrhoeae GyrA and the residue analogous to (6a)-(6e) (above);

(8) bacteria (VII) comprising a protein that is at least 30% identical to the sequence of the N. gonorrhoeae FabI protein in which the amino acid residue corresponding to:

(a) 15 is Val;

(b) 20 is Thr;

(c) 23 is Gly;

(d) 25 is Val;

(e) 51 is Thr;

(f) 91 is Thr;

(g) 93 is Cys or Ser;

(h) 95 is Val;

(i) 104 is Leu;

(j) 105 is His;

(k) 144 is Val;

(l) 147 is His;

(m) 159 is Ala;

(n) 160 is isoLeu;

(o) 162 is Val;

(p) 193 is Asp or Val;

(q) 201 is Val;

(r) 203 is Tyr or Val;

(s) 204 is Ser, Leu, isoLeu or Val;

(t) 212 is Thr or Val; or

(u) 247 is Asp;

(9) a protein (VIII) comprising a sequence at least 30% identical to the sequence of N. gonorrhoeae FabI protein comprising the amino acids (8a)-(8u); and

(10) a process for screening compounds for antibacterial activity comprising:

(a) generating DNA fragments by PCR amplification of DNA from the entire genome of a bacteria under conditions that allow for mutation of the fragments;

(b) allowing 1 or more of the generated PCR fragments to be

incorporated into the chromosome of a bacteria by homologous recombination;

(c) isolating the bacteria that demonstrate resistance to an antibacterial compound;

(d) identifying the mutation contained in the DNA fragment;

(e) contacting the bacteria with compounds; and

(f) evaluating the compounds for antibacterial activity.

USE - The methods are used for identifying and characterizing drug-target interactions (claimed). The antibacterial strains generated can be used to provide information that could be used or developed for treating bacterial infections of humans, other animals and plants.

ADVANTAGE - The mutations provide valuable information about the molecular target of a compound and how the target and compound interact. The methods allow the simultaneous creation and identification of mutations that confer resistance to antibacterial compounds.

Dwg.0/4

L5 ANSWER 11 OF 29 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-148084 [14] WPIDS
CROSS REFERENCE: 2000-161479 [49]
DOC. NO. CPI: C2000-046503
TITLE: Design of antibiotics for inhibition of microorganism cell division comprises testing for compounds which block the s-adenosylmethionine-dependent step of crosswall formation during cell division.
DERWENT CLASS: B04 D16
INVENTOR(S): NEWMAN, E B
PATENT ASSIGNEE(S): (NEWM-I) NEWMAN E B
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 2255460	A1	19990615	(200014)*	EN	28

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 2255460	A1	CA 1998-2255460	19981211

PRIORITY APPLN. INFO: CA 1997-2224776 19971215
AB CA 2255460 A UPAB: 20000323

NOVELTY - Designing antibiotics comprises testing compounds which inhibit microorganism cell division by blocking the s-adenosylmethionine (SAM)-dependent step of formation of crosswall during cell division in microorganisms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method to screen genes and proteins which require modification by SAM comprising:

(a) cloning genes coding for prospective targets on a variable expression vector; and

(b) determining an inducer level which produces filamentation; and

(2) a method to screen compounds for their ability to inhibit the SAM-dependent step comprising:

(a) producing filaments in metK cells carrying a fstZ-green fluorescent protein fusion; and

(b) determining a rate of constriction of the fstZ ring and the conversion of filaments to normal cells in the presence of compounds of interest.

USE - These tests identify a new target for antibiotic design, the yabC gene product which catalyzes the SAM-dependent step. Compounds which induce or repress the yabBC promoter or increase production of the yabC gene product and inhibitors of the yabC SAM-dependent methylase can be used as antibiotics.

Dwg.0/2

L5 ANSWER 12 OF 29 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-126438 [11] WPIDS
CROSS REFERENCE: 2000-105801 [09]; 2000-105811 [09]; 2000-105814 [09]; 2000-105815 [09]; 2000-105826 [09]; 2000-105827 [09]; 2000-105828 [09]; 2000-105829 [09]; 2000-116431 [10]; 2000-116432 [10]; 2000-116448 [10]; 2000-116449 [10]; 2000-116450 [10]; 2000-116451 [10]; 2000-116452 [10]; 2000-116453 [10]; 2000-126427 [11]; 2000-126428 [11]; 2000-126429 [11]; 2000-126430 [11]; 2000-126435 [11]; 2000-126436 [11]; 2000-126437 [11]; 2000-126439 [11]; 2000-126440 [11]; 2000-136825 [12]; 2000-136826 [12]; 2000-136829 [12]; 2000-136830 [12]; 2000-136831 [12]; 2000-147073 [13]; 2000-147074 [13]; 2000-147075 [13]; 2000-160447 [14]; 2000-160448 [14]; 2000-160453 [14]; 2000-160454 [14]; 2000-170778 [15]; 2000-181984 [16]; 2000-181985 [16]; 2000-181986 [16]; 2000-182022 [16]; 2000-328378 [28]; 2002-672820 [72]
DOC. NO. NON-CPI: N2000-095317
DOC. NO. CPI: C2000-038458
TITLE: New multibinding compounds with enhanced biological and/or therapeutic effect (e.g. increased specificity, potency, efficacy and duration of action), useful as antibacterial agents and in animal feed to improve growth of livestock.
DERWENT CLASS: B05 S03
INVENTOR(S): FATHEREE, P; GRIFFIN, J H; JUDICE, J K; PACE, J L
PATENT ASSIGNEE(S): (ADME-N) ADVANCED MEDICINE INC
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9964051	A1	19991216	(200011)*	EN	102
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9944266	A	19991230	(200022)		
EP 1083920	A1	20010321	(200117)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9964051	A1	WO 1999-US12779	19990607
AU 9944266	A	AU 1999-44266	19990607

EP 1083920 A1 EP 1999-927332 19990607
WO 1999-US12779 19990607

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9944266	A	Based on	WO 9964051
EP 1083920	A1	Based on	WO 9964051

PRIORITY APPLN. INFO: US 1998-93072P 19980716; US 1998-88448P 19980608

AB WO 9964051 A UPAB: 20021113

NOVELTY - Multibinding compounds (I) and their salts are new.

DETAILED DESCRIPTION - Multibinding compounds of formula (I) and their salts are new.

L = ligand comprising ligand domain capable of **inhibiting** bacterial Type II **DNA** topoisomerase;

X = linker;

p = 2-10; and

q = 1-20.

INDEPENDENT CLAIMS are also included for:

(1) a method for identifying multimeric ligand compounds that possess multibinding properties with respect to bacterial Type II **DNA** topoisomerase;

(2) library of multimeric ligand compounds that may possess multibinding properties with respect to bacterial Type II **DNA** topoisomerase.

ACTIVITY - Antibacterial.

Antibacterial activity of test compounds (I) was determined in vitro using **DNA** biosynthesis assay in E. coli H560 cells. Duplicate test samples were blank (boiled cells or cells + TCA or buffer with no cells), control without ATP, control with ATP, test compounds (0.2, 1, 5, 20, 100 and 40 mu g/ml) all with ATP. Test compounds (I) were active in this test.

MECHANISM OF ACTION - Bacterial Type II **DNA** topoisomerase **inhibitor.**

USE - Used to treat pathologic conditions alleviated by treatment with antibacterial agents (claimed). Used in animal feed to improve growth of livestock.

ADVANTAGE - Enhanced biological and/or therapeutic effects (e.g. increased specificity, affinity, selectivity, potency, efficacy and therapeutic index, change in duration of action, decreased toxicity and side-effects and improved bioavailability, pharmacokinetics and activity spectrum) compared with prior art compounds. Active against broad spectrum of **bacteria**, particularly **bacteria** resistant to existing drug therapy, and have high activity and selectivity towards their targets. Bind efficiently to mutant topoisomerases because of reduced energetics of the interaction.

Dwg.0/0

L5 ANSWER 13 OF 29 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1990-051727 [07] WPIDS
CROSS REFERENCE: 1992-066623 [09]
DOC. NO. CPI: C1990-022438
TITLE: Treatment of bacterial infections and identification of bacteria - using anti-sense oligo nucleotide antibiotics

complementary to macromolecular synthesis operon.
DERWENT CLASS: B04 D16
INVENTOR(S): LUPSKI, J R
PATENT ASSIGNEE(S): (BAYU) BAYLOR COLLEGE MEDICINE
COUNTRY COUNT: 14
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9000624	A	19900125	(199007)*	EN	36
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU JP					
AU 8937844	A	19900111	(199017)		
AU 8941808	A	19900205	(199032)		
EP 424473	A	19910502	(199118)		
R: AT BE CH DE FR GB IT LU NL SE					
JP 03505672	W	19911212	(199205)		
AU 633495	B	19930204	(199312)		
EP 424473	B1	19960508	(199623)	EN	14
R: AT BE CH DE FR GB IT LI NL SE					
DE 68926455	E	19960613	(199629)		
CA 1340796	C	19991019	(200009)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9000624	A	WO 1989-US2884	19890630
EP 424473	A	EP 1989-906671	19890630
JP 03505672	W	JP 1989-509036	19890630
AU 633495	B	AU 1989-37844	19890705
EP 424473	B1	EP 1989-909671	19890630
		WO 1989-US2884	19890630
DE 68926455	E	DE 1989-626455	19890630
		EP 1989-909671	19890630
		WO 1989-US2884	19890630
CA 1340796	C	CA 1989-604846	19890705

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 633495	B	Previous Publ.	AU 8937844
EP 424473	B1	Based on	WO 9000624
DE 68926455	E	Based on	EP 424473
		Based on	WO 9000624

PRIORITY APPLN. INFO: US 1988-215135 19880705
AB WO 9000624 A UPAB: 20000218
Method of interrupting the expression of a macromolecular synthesis (MMS) operon comprises binding an antisense oligonucleotide to an mRNA transcribed from the MMS operon. Also claimed is a method of identifying bacteria by binding a unique intergenic antisense oligonucleotide to a mRNA transcribed from an MMS operon and determining the amt. of the binding. New antibiotic comprises at least a 10 mer oligonucleotide (I) which is complementary to a sense strand of an MMS operon and binds to a mRNA transcribed by the sense strand. Also claimed are methods of treating
bacterial infections by (1) competitively **inhibiting** a recognition site of a protein encoded by an MMS operon by introducing a

competitive oligonucleotide into a bacterium, or (2) interrupting the function of proteins S21, primase or sigma-70. To identify, an MMS operon is treated to form single-stranded **DNA**; an antisense oligonucleotide is bound to a unique intergenic sequence in the single stranded **DNA** of the MMS operon; and the amt. of binding is measured.

USE/ADVANTAGE - By interrupting the expression of the MMS operon, bacterial infections can be treated. By binding of (I) specifically to a unique sequence in the intergenic regions of the MMS operon of **bacteria**, **bacteria** may be identified. By competitive **inhibition** of the MMS operon gene prods. by using oligonucleotides known to act as recognition sequences for the MMS operon protein prods., bacterial infections may also be treated.

operon
protein
prods.,
bacterial
infections
may
also
be treated.
Dwg.0/7
Dwg.0/7

L5 ANSWER 14 OF 29 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1989-304907 [42] WPIDS
DOC. NO. CPI: C1989-134995
TITLE: Recombinant plasmid contg. marked specific gene - used to construct bacteria used for nitrogen fixing.
DERWENT CLASS: C03 D16
PATENT ASSIGNEE(S): (KYOW) KYOWA HAKKO KOGYO KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 01225483	A	19890908	(198942)*		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 01225483	A	JP 1988-49867	19880304

PRIORITY APPLN. INFO: JP 1988-49867 19880304
AB JP 01225483 A UPAB: 19930923
Recombinant **plasmid** contains nif L gene defected with marker and a nif A gene and promoter integrated upstream of the nif A gene. The recombinant **plasmid** is pNOY9Cm.

Klebsiella sp. bacteria which has N-fixing ability, has a defected nif L gene on the chromosome, a promoter integrated upstream of the nif A gene, and **inhibition** of the N-fixing ability in the presence of ammonia is reduced. The bacteria is Klebsiella oxytoca R16.

Jkevsuekka so, bacteria contains more recombinant **plasmid** integrated by a promoter upstream of the nif A gene. The bacteria is Klebsiella oxytoca R16 (pNOA102).

USE/ADVANTAGE - Bacteria is useful for N-fixing, and the recombinant **plasmid** is used for construction of the **bacteria**. The

bacteria expresses N-fixing ability completely.
0/0

L5 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:534133 BIOSIS
DOCUMENT NUMBER: PREV200200534133
TITLE: Review article: The role of the gut flora in health and disease, and its modification as therapy.
AUTHOR(S): Hart, A. L.; Stagg, A. J.; Frame, M.; Graffner, H.; Glise, H.; Falk, P.; Kamm, M. A. (1)
CORPORATE SOURCE: (1) St Mark's Hospital, Watford Road, Harrow, Middlesex, HA1 3UJ: kamm@ic.ac.uk UK
SOURCE: Alimentary Pharmacology & Therapeutics, (August, 2002) Vol. 16, No. 8, pp. 1383-1393. http://www.blackwell-science.com/apt. print.
ISSN: 0269-2813.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB The gut flora is a vast interior ecosystem whose nature is only beginning to be unravelled, due to the emergence of sophisticated molecular tools. Techniques such as 16S ribosomal RNA analysis, polymerase chain reaction amplification and the use of **DNA** microarrays now facilitate rapid identification and characterization of species resistant to conventional culture and possibly unknown species. Life-long cross-talk between the host and the gut flora determines whether health is maintained or disease intervenes. An understanding of these **bacteria**-**bacteria** and **bacteria**-host immune and epithelial cell interactions is likely to lead to a greater insight into disease pathogenesis. Studies of single organism-epithelial interactions have revealed the large range of metabolic processes that gut bacteria may influence. In inflammatory bowel diseases, bacteria drive the inflammatory process, and genetic predisposition to disease identified to date, such as the recently described NOD2/CARD15 gene variants, may relate to altered bacterial recognition. Extra-intestinal disorders, such as atopy and arthritis, may also have an altered gut milieu as their basis. Clinical evidence is emerging that the modification of this internal environment, using either antibiotics or probiotic bacteria, is beneficial in **preventing** and treating disease. This natural and apparently safe approach holds great appeal.

L5 ANSWER 16 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:424364 BIOSIS
DOCUMENT NUMBER: PREV200000424364
TITLE: Development of a direct viable count procedure for the investigation of VBNC state in Listeria monocytogenes.
AUTHOR(S): Besnard, V.; Federighi, M.; Cappelier, J. M. (1)
CORPORATE SOURCE: (1) Unite Mixte de Recherches hygiene des aliments INRA-ENVN, Ecole Nationale Veterinaire de Nantes, Route de Gachet, 44307, Nantes France
SOURCE: Letters in Applied Microbiology, (July, 2000) Vol. 31, No. 1, pp. 77-81. print.
ISSN: 0266-8254.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A viable but non-culturable (VBNC) bacterial state was originally detected

in studies in environmental microbiology. In particular, this state has been demonstrated for a number of human pathogens (Escherichia coli, Salmonella enteritidis, Vibrio cholerae, Legionella pneumophila and Campylobacter jejuni). The presence of VBNC cells poses a major public health problem since they cannot be detected by traditional culturing methods and the cells remain potentially pathogenic under favourable conditions. But, as far as we know, the VBNC state has not been yet described in Listeria monocytogenes. In most studies, this has been assessed by the Kogure procedure based on cellular elongation in the presence of **DNA** gyrase **inhibitors**. The antibiotic used was nalidixic acid in order to **prevent DNA** replication, only efficient in Gram-negative bacteria studies. In this study, we describe a new DVC procedure to detect and count viable of L. monocytogenes suspended in filtered, sterilized distilled water. We used different concentrations of ciprofloxacin, efficient both in Gram-negative and Gram-positive **bacteria**. **Bacteria** cells were removed and resuspended in BHI broth, with yeast extract and ciprofloxacin. The mixture was incubated at different incubation times at 37degreeC. After different incubation times, cells were filtered through an isopore polycarbonate black membrane filter and covered with a DAPI solution or orange acridine. The filters were prepared and examined by epifluorescence microscopy. Elongated cells were counted as viable cells, whereas normal size was regarded as nonactive ones. This method allows determination of ciprofloxacin concentration and incubation time optimal to detect maximum viable cells percentage in L. monocytogenes.

L5 ANSWER 17 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:33778 BIOSIS
DOCUMENT NUMBER: PREV199497046778
TITLE: Characterization of fimbriae produced by enteropathogenic Escherichia coli.
AUTHOR(S): Giron, Jorge A. (1); Ho, Alice Suk Yue; Schoolnik, Gary K.
CORPORATE SOURCE: (1) Cent. Vaccine Development, Univ. Maryland, 10 South Pine Street, Baltimore, MD 21201 USA
SOURCE: Journal of Bacteriology, (1993) Vol. 175, No. 22, pp. 7391-7403.
ISSN: 0021-9193.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Enteropathogenic Escherichia coli (EPEC) express rope-like bundles of filaments, termed bundle-forming pili (BFP) (J. A. Giron, A. S. Y. Ho, and G. K. Schoolnik, Science 254:710-713, 1991). Expression of BFP is associated with localized adherence to HEp-2 cells and the presence of the EPEC adherence factor **plasmid**. In this study, we describe the identification of rod-like fimbriae and fibrillae expressed simultaneously on the bacterial surface of three prototype EPEC strains. Upon fimbrial extraction from EPEC B171 (O111:NM), three fimbrial subunits with masses of 16.5, 15.5, and 14.7 kDa were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Their N-terminal amino acid sequence showed homology with F9 and F7-2 fimbriae of uropathogenic E. coli and F1845 of diffuse-adhering E. coli, respectively. The mixture of fimbrial subunits (called FB171) exhibited mannose-resistant agglutination of human erythrocytes only, and this activity was not **inhibited** by alpha-D-Gal(1-4)-beta-Gal disaccharide or any other described receptor analogs for P, S, F, M, G, and Dr hemagglutinins of uropathogenic E. coli,

which suggests a different receptor specificity. Hemagglutination was **inhibited** by extracellular matrix glycoproteins, i.e., collagen type IV, laminin, and fibronectin, and to a lesser extent by gangliosides, fetuin, and asialofetuin. Scanning electron microscopic studies performed on clusters of bacteria adhering to HEp-2 cells revealed the presence of structures resembling BFP and rod-like fimbriae linking **bacteria** to **bacteria** and **bacteria** to the eukaryotic cell membrane. We suggest a role of these surface appendages in the interaction of EPEC with eukaryotic cells as well as in the overall pathogenesis of intestinal disease caused by EPEC.

L5 ANSWER 18 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1987:207625 BIOSIS
DOCUMENT NUMBER: BA83:105255
TITLE: ANTIBACTERIAL ACTIVITY AND MECHANISM OF ACTION OF 3' AZIDO-3'-DEOXYTHYMIDINE BWA-509U.
AUTHOR(S): ELWELL L P; FERONE R; FREEMAN G A; FYFE J A; HILL J A; RAY P H; RICHARDS C A; SINGER S C; KNICK V B; ET AL
CORPORATE SOURCE: DEP. MICROBIOLOGY, WELLCOME RES. LAB., RESEARCH TRIANGLE PARK, NC 27709.
SOURCE: ANTIMICROB AGENTS CHEMOTHER, (1987) 31 (2), 274-280. CODEN: AMACCQ. ISSN: 0066-4804.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The thymidine analog 3'-azido-3'-deoxythymidine (BWA509U; azidothymidine [AZT]) had potent bactericidal activity against many members of the family Enterobacteriaceae, including strains of Escherichia coli, Salmonella typhimurium, Klebsiella pneumoniae, Shigella flexneri, and Enterobacter aerogenes. AZT also had bactericidal activity against Vibrio cholerae and the fish pathogen Vibrio anguillarum. AZT had no activity against Pseudomonas aeruginosa, gram-positive **bacteria**, anaerobic **bacteria**, Mycobacterium tuberculosis, nontuberculosis mycobacteria, or most fungal pathogens. Several lines of evidence indicated that AZT must be activated to the nucleotide level to **inhibit** cellular metabolism: (i) AZT was a substrate for Escherichia coli thymidine kinase; (ii) spontaneously arising AZT-resistant mutants of E. coli ML-30 and S. typhimurium were deficient in thymidine kinase; and (iii) intact E. coli ML-30 cells converted [3H]AZT to its mono-, di-, and triphosphate metabolites. Of the phosphorylated metabolites, AZT-5'-triphosphate was the most potent **inhibitor** of replicative **DNA** synthesis in toluene-permeabilized E. coli pol A mutant cells. AZT-treated E. coli cultures grown in minimal medium contained highly elongated cells consistent with the **inhibition** of **DNA** synthesis. AZT-triphosphate was a specific **DNA** chain terminator in the in vitro **DNA** polymerization reaction catalyzed by the Klenow fragment of E. coli **DNA** polymerase 1. Thus, **DNA** chain termination may explain the lethal properties of this compound against susceptible microorganisms.

L5 ANSWER 19 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1985:306079 BIOSIS
DOCUMENT NUMBER: BA79:86075
TITLE: FURTHER CHARACTERIZATION OF REPAIR OF 8 METHOXYPSORALEN CROSSLINKS IN UV-EXCISION-DEFECTIVE ESCHERICHIA-COLI.
AUTHOR(S): BRIDGES B A
CORPORATE SOURCE: MRC CELL MUTATION UNIT, UNIV. SUSSEX, FALMER, BRIGHTON,

SUSSEX BN1 9RR, GREAT BRITAIN.
SOURCE: MUTAT RES, (1984 (RECD 1985)) 132 (5-6), 153-160.
CODEN: MUREAV. ISSN: 0027-5107.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Evidence was previously presented for a new pathway for the repair of 8-methoxypsoralen **DNA** crosslinks. The pathway, which is independent of the uvrA gene but deficient in rep mutants, was now further characterized and shown to be more active in minimal than in nutrient growth media and to be **inhibited** by acriflavine. Although crosslink repair is much reduced in recA bacteria, some still occurs as judged by the effect of acriflavine. By the same criterion, crosslink repair occurs in bacteria with point mutations in the uvrA and uvrB genes, in bacteria with a deletion covering the uvrB gene, and in polA uvrA **bacteria**. **Bacteria** with insertions rather than point mutations in the uvrA gene, although showing evidence of repair, demonstrated minimal **inhibition** with acriflavine suggesting the possibility that the uvrA gene product, even if enzymically inactive, might be able to interact with **DNA** lesions in the presence of acriflavine and **prevent** crosslink repair. Crosslink repair in E. coli WP2 uvrA is associated with base-pair substitution mutagenesis and may be characterized as an error-prone process. Crosslink repair in uvrA bacteria is reduced but not eliminated by a mutation in the umuC gene.

L5 ANSWER 20 OF 29 MEDLINE
ACCESSION NUMBER: 2002426080 MEDLINE
DOCUMENT NUMBER: 22170281 PubMed ID: 12182739
TITLE: The role of the gut flora in health and disease, and its modification as therapy.
AUTHOR: Hart A L; Stagg A J; Frame M; Graffner H; Glise H; Falk P; Kamm M A
CORPORATE SOURCE: St. Mark's Hospital, Harrow, Middlesex, UK.
SOURCE: ALIMENTARY PHARMACOLOGY AND THERAPEUTICS, (2002 Aug) 16 (8) 1383-93. Ref: 92
Journal code: 8707234. ISSN: 0269-2813.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20020817
Last Updated on STN: 20030215
Entered Medline: 20030214
AB The gut flora is a vast interior ecosystem whose nature is only beginning to be unravelled, due to the emergence of sophisticated molecular tools. Techniques such as 16S ribosomal RNA analysis, polymerase chain reaction amplification and the use of **DNA** microarrays now facilitate rapid identification and characterization of species resistant to conventional culture and possibly unknown species. Life-long cross-talk between the host and the gut flora determines whether health is maintained or disease intervenes. An understanding of these **bacteria**-**bacteria** and **bacteria**-host immune and epithelial cell interactions is likely to lead to a greater insight into disease pathogenesis. Studies of single organism-epithelial interactions have

revealed the large range of metabolic processes that gut bacteria may influence. In inflammatory bowel diseases, bacteria drive the inflammatory process, and genetic predisposition to disease identified to date, such as the recently described NOD2/CARD15 gene variants, may relate to altered bacterial recognition. Extra-intestinal disorders, such as atopy and arthritis, may also have an altered gut milieu as their basis. Clinical evidence is emerging that the modification of this internal environment, using either antibiotics or probiotic bacteria, is beneficial in **preventing** and treating disease. This natural and apparently safe approach holds great appeal.

L5 ANSWER 21 OF 29 MEDLINE
ACCESSION NUMBER: 2000417319 MEDLINE
DOCUMENT NUMBER: 20344504 PubMed ID: 10886620
TITLE: Development of a direct viable count procedure for the investigation of VBNC state in Listeria monocytogenes.
AUTHOR: Besnard V; Federighi M; Cappelier J M
CORPORATE SOURCE: Unite Mixte de Recherches hygiene des aliments INRA-ENVN, Ecole Nationale Veterinaire de Nantes, Route de Gachet, NANTES, France.
SOURCE: LETTERS IN APPLIED MICROBIOLOGY, (2000 Jul) 31 (1) 77-81.

Journal code: 8510094. ISSN: 0266-8254.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000901

AB A viable but non-culturable (VBNC) bacterial state was originally detected in studies in environmental microbiology. In particular, this state has been demonstrated for a number of human pathogens (Escherichia coli, Salmonella enteritidis, Vibrio cholerae, Legionella pneumophila and Campylobacter jejuni). The presence of VBNC cells poses a major public health problem since they cannot be detected by traditional culturing methods and the cells remain potentially pathogenic under favourable conditions. But, as far as we know, the VBNC state has not been yet described in Listeria monocytogenes. In most studies, this has been assessed by the Kogure procedure based on cellular elongation in the presence of **DNA** gyrase **inhibitors**. The antibiotic used was nalidixic acid in order to **prevent DNA** replication, only efficient in Gram-negative bacteria studies. In this study, we describe a new DVC procedure to detect and count viable of L. monocytogenes suspended in filtered, sterilized distilled water. We used different concentrations of ciprofloxacin, efficient both in Gram-negative and Gram-positive **bacteria**. **Bacteria** cells were removed and resuspended in BHI broth, with yeast extract and ciprofloxacin. The mixture was incubated at different incubation times at 37 degrees C. After different incubation times, cells were filtered through an isopore polycarbonate black membrane filter and covered with a DAPI solution or orange acridine. The filters were prepared and examined by epifluorescence microscopy. Elongated cells were counted as viable cells, whereas normal size was regarded as nonactive ones. This method allows determination of ciprofloxacin concentration and incubation time

optimal to detect maximum viable cells percentage in L. monocytogenes.

L5 ANSWER 22 OF 29 MEDLINE
ACCESSION NUMBER: 94042915 MEDLINE
DOCUMENT NUMBER: 94042915 PubMed ID: 7901197
TITLE: Characterization of fimbriae produced by enteropathogenic Escherichia coli.
AUTHOR: Giron J A; Ho A S; Schoolnik G K
CORPORATE SOURCE: Department of Microbiology and Immunology, Howard Hughes Medical Institute, Stanford University, California 94305.
CONTRACT NUMBER: DK 38707 (NIDDK)
SOURCE: JOURNAL OF BACTERIOLOGY, (1993 Nov) 175 (22) 7391-403. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931214

AB Enteropathogenic Escherichia coli (EPEC) express rope-like bundles of filaments, termed bundle-forming pili (BFP) (J. A. Giron, A. S. Y. Ho, and G. K. Schoolnik, Science 254:710-713, 1991). Expression of BFP is associated with localized adherence to HEp-2 cells and the presence of the EPEC adherence factor **plasmid**. In this study, we describe the identification of rod-like fimbriae and fibrillae expressed simultaneously on the bacterial surface of three prototype EPEC strains. Upon fimbrial extraction from EPEC B171 (O111:NM), three fimbrial subunits with masses of 16.5, 15.5, and 14.7 kDa were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Their N-terminal amino acid sequence showed homology with F9 and F7(2) fimbriae of uropathogenic E. coli and F1845 of diffuse-adhering E. coli, respectively. The mixture of fimbrial subunits (called FB171) exhibited mannose-resistant agglutination of human erythrocytes only, and this activity was not **inhibited** by alpha-D-Gal(1-4)-beta-Gal disaccharide or any other described receptor analogs for P, S, F, M, G, and Dr hemagglutinins of uropathogenic E. coli, which suggests a different receptor specificity. Hemagglutination was **inhibited** by extracellular matrix glycoproteins, i.e., collagen type IV, laminin, and fibronectin, and to a lesser extent by gangliosides, fetuin, and asialofetuin. Scanning electron microscopic studies performed on clusters of bacteria adhering to HEp-2 cells revealed the presence of structures resembling BFP and rod-like fimbriae linking **bacteria** to **bacteria** and **bacteria** to the eukaryotic cell membrane. We suggest a role of these surface appendages in the interaction of EPEC with eukaryotic cells as well as in the overall pathogenesis of intestinal disease caused by EPEC.

L5 ANSWER 23 OF 29 MEDLINE
ACCESSION NUMBER: 87183451 MEDLINE
DOCUMENT NUMBER: 87183451 PubMed ID: 3551832
TITLE: Antibacterial activity and mechanism of action of 3'-azido-3'-deoxythymidine (BW A509U).

AUTHOR: Elwell L P; Ferone R; Freeman G A; Fyfe J A; Hill J A; Ray P H; Richards C A; Singer S C; Knick V B; Rideout J L; +
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1987 Feb) 31 (2) 274-80.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198705
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870520

AB The thymidine analog 3'-azido-3'-deoxythymidine (BW A509U; azidothymidine [AZT]) had potent bactericidal activity against many members of the family Enterobacteriaceae, including strains of Escherichia coli, Salmonella typhimurium, Klebsiella pneumoniae, Shigella flexneri, and Enterobacter aerogenes. AZT also had bactericidal activity against Vibrio cholerae and the fish pathogen Vibrio anguillarum. AZT had no activity against Pseudomonas aeruginosa, gram-positive **bacteria**, anaerobic **bacteria**, Mycobacterium tuberculosis, nontuberculosis mycobacteria, or most fungal pathogens. Several lines of evidence indicated that AZT must be activated to the nucleotide level to **inhibit** cellular metabolism: AZT was a substrate for E. coli thymidine kinase; spontaneously arising AZT-resistant mutants of E. coli ML-30 and S. typhimurium were deficient in thymidine kinase; and intact E. coli ML-30 cells converted [3H]AZT to its mono-, di-, and triphosphate metabolites. Of the phosphorylated metabolites, AZT-5'-triphosphate was the most potent **inhibitor** of replicative **DNA** synthesis in toluene-permeabilized E. coli pol A mutant cells. AZT-treated E. coli cultures grown in minimal medium contained highly elongated cells consistent with the **inhibition** of **DNA** synthesis. AZT-triphosphate was a specific **DNA** chain terminator in the in vitro **DNA** polymerization reaction catalyzed by the Klenow fragment of E. coli **DNA** polymerase I. Thus, **DNA** chain termination may explain the lethal properties of this compound against susceptible microorganisms.

L5 ANSWER 24 OF 29 MEDLINE
ACCESSION NUMBER: 85086074 MEDLINE
DOCUMENT NUMBER: 85086074 PubMed ID: 6096705
TITLE: Further characterization of repair of 8-methoxypsoralen crosslinks in UV-excision-defective Escherichia coli.
AUTHOR: Bridges B A
SOURCE: MUTATION RESEARCH, (1984 Nov-Dec) 132 (5-6) 153-60.
Journal code: 0400763. ISSN: 0027-5107.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198502
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850208

AB Evidence was previously presented for a new pathway for the repair of 8-methoxypsoralen **DNA** crosslinks. The pathway, which is independent of the uvrA gene but deficient in rep mutants, has now been further characterized and shown to be more active in minimal than in

nutrient growth media and to be **inhibited** by acriflavine. Although crosslink repair is much reduced in recA bacteria, some still occurs as judged by the effect of acriflavine. By the same criterion, crosslink repair occurs in bacteria with point mutations in the uvrA and uvrB genes, in bacteria with a deletion covering the uvrB gene, and in polA uvrA **bacteria**. **Bacteria** with insertions rather than point mutations in the uvrA gene, although showing evidence of repair, demonstrated minimal **inhibition** with acriflavine suggesting the possibility that the uvrA gene product, even if enzymically inactive, might be able to interact with **DNA** lesions in the presence of acriflavine and **prevent** crosslink repair. Crosslink repair in E. coli WP2 uvrA is associated with base-pair substitution mutagenesis and may be characterized as an error-prone process. Crosslink repair in uvrA bacteria is reduced but not eliminated by a mutation in the umuC gene.

L5 ANSWER 25 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002309976 EMBASE

TITLE: Review article: The role of the gut flora in health and disease, and its modification as therapy.

AUTHOR: Hart A.L.; Stagg A.J.; Frame M.; Graffner H.; Glise H.; Falk P.; Kamm M.A.

CORPORATE SOURCE: Prof. M.A. Kamm, St Mark's Hospital, Watford Road, Harrow, Middlesex HA1 3UJ, United Kingdom. kamm@ic.ac.uk

SOURCE: Alimentary Pharmacology and Therapeutics, (2002) 16/8 (1383-1393).
Refs: 92
ISSN: 0269-2813 CODEN: APTHEN

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The gut flora is a vast interior ecosystem whose nature is only beginning to be unravelled, due to the emergence of sophisticated molecular tools. Techniques such as 16S ribosomal RNA analysis, polymerase chain reaction amplification and the use of **DNA** microarrays now facilitate rapid identification and characterization of species resistant to conventional culture and possibly unknown species. Life-long cross-talk between the host and the gut flora determines whether health is maintained or disease intervenes. An understanding of these **bacteria**-**bacteria** and **bacteria**-host immune and epithelial cell interactions is likely to lead to a greater insight into disease pathogenesis. Studies of single organism-epithelial interactions have revealed the large range of metabolic processes that gut bacteria may influence. In inflammatory bowel diseases, bacteria drive the inflammatory process, and genetic predisposition to disease identified to date, such as the recently described NOD2/CARD15 gene variants, may relate to altered bacterial recognition. Extra-intestinal disorders, such as atopy and arthritis, may also have an altered gut milieu as their basis. Clinical evidence is emerging that the modification of this internal environment, using either antibiotics or probiotic bacteria, is beneficial in

preventing and treating disease. This natural and apparently safe approach holds great appeal.

L5 ANSWER 26 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000251922 EMBASE
TITLE: Development of a direct viable count procedure for the investigation of VBNC state in Listeria monocytogenes.
AUTHOR: Besnard V.; Federighi M.; Cappelier J.M.
CORPORATE SOURCE: J.M. Cappelier, Unite Mixte Recher. hygiene aliments, INRA-ENVN, Ecole Natl. Veterinaire de Nantes, Route de Gachet, 44307 Nantes, France. cappelier@vet-nantes.fr
SOURCE: Letters in Applied Microbiology, (2000) 31/1 (77-81). Refs: 22
ISSN: 0266-8254 CODEN: LAMIE7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB V. BESNARD, M. FEDERIGHI AND J.M. CAPPELIER. 2000 A viable but non-culturable (VBNC) bacterial state was originally detected in studies in environmental microbiology. In particular, this state has been demonstrated for a number of human pathogens (Escherichia coli, Salmonella enteritidis, Vibrio cholerae, Legionella pneumophila and Campylobacter jejuni). The presence of VBNC cells poses a major public health problem since they cannot be detected by traditional culturing methods and the cells remain potentially pathogenic under favourable conditions. But, as far as we know, the VBNC state has not been yet described in Listeria monocytogenes. In most studies, this has been assessed by the Kogure procedure based on cellular elongation in the presence of **DNA** gyrase **inhibitors**. The antibiotic used was nalidixic acid in order to **prevent DNA** replication, only efficient in Gram-negative bacteria studies. In this study, we describe a new DVC procedure to detect and count viable of L. monocytogenes suspended in filtered, sterilized distilled water. We used different concentrations of ciprofloxacin, efficient both in Gram-negative and Gram-positive **bacteria**. **Bacteria** cells were removed and resuspended in BHI broth, with yeast extract and ciprofloxacin. The mixture was incubated at different incubation times at 37.degree.C. After different incubation times, cells were filtered through an isopore polycarbonate black membrane filter and covered with a DAPI solution or orange acridine. The filters were prepared and examined by epifluorescence microscopy. Elongated cells were counted as viable cells, whereas normal size was regarded as nonactive ones. This method allows determination of ciprofloxacin concentration and incubation time optimal to detect maximum viable cells percentage in L. monocytogenes.

L5 ANSWER 27 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93339334 EMBASE
DOCUMENT NUMBER: 1993339334
TITLE: Characterization of fimbriae produced by enteropathogenic Escherichia coli.
AUTHOR: Giron J.A.; Ho A.S.Y.; Schoolnik G.K.
CORPORATE SOURCE: Center for Vaccine Development, University of Maryland, 10 South Pine St.,Baltimore, MD 21201, United States
SOURCE: Journal of Bacteriology, (1993) 175/22 (7391-7403).
ISSN: 0021-9193 CODEN: JOBAAY

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Enteropathogenic Escherichia coli (EPEC) express rope-like bundles of filaments, termed bundle-forming pili (BFP) (J. A. Giron, A. S. Y. Ho, and G. K. Schoolnik, Science 254:710-713, 1991). Expression of BFP is associated with localized adherence to HEp-2 cells and the presence of the EPEC adherence factor **plasmid**. In this study, we describe the identification of rod-like fimbriae and fibrillae expressed simultaneously on the bacterial surface of three prototype EPEC strains. Upon fimbrial extraction from EPEC B171 (O111:NM), three fimbrial subunits with masses of 16.5, 15.5, and 14.7 kDa were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Their N-terminal amino acid sequence showed homology with F9 and F72 fimbriae of uropathogenic E. coli and F1845 of diffuse-adhering E. coli, respectively. The mixture of fimbrial subunits (called FB171) exhibited mannose-resistant agglutination of human erythrocytes only, and this activity was not **inhibited** by .alpha.-D-Gal(1-4)-.beta.-Gal disaccharide or any other described receptor analogs for P, S, F, M, G, and Dr hemagglutinins of uropathogenic E. coli, which suggests a different receptor specificity. Hemagglutination was **inhibited** by extracellular matrix glycoproteins, i.e., collagen type IV, laminin, and fibronectin, and to a lesser extent by gangliosides, fetuin, and asialofetuin. Scanning electron microscopic studies performed on clusters of bacteria adhering to HEp-2 cells revealed the presence of structures resembling BFP and rod-like fimbriae linking **bacteria** to **bacteria** and **bacteria** to the eukaryotic cell membrane. We suggest a role of these surface appendages in the interaction of EPEC with eukaryotic cells as well as in the overall pathogenesis of intestinal disease caused by EPEC.

L5 ANSWER 28 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87078751 EMBASE
DOCUMENT NUMBER: 1987078751
TITLE: Antibacterial activity and mechanism of action of 3'-azido-3'-deoxythymidine (BW A509U).
AUTHOR: Elwell L.P.; Ferone R.; Freeman G.A.; et al.
CORPORATE SOURCE: Department of Microbiology, Wellcome Research Laboratories, Research Triangle Park, NC 27709, United States
SOURCE: Antimicrobial Agents and Chemotherapy, (1987) 31/2 (274-280).
CODEN: AMACCQ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
004 Microbiology
006 Internal Medicine
LANGUAGE: English

AB The thymidine analog 3'-azido-3'-deoxythymidine (BW A509U; azidothymidine

[AZT]) had potent bactericidal activity against many members of the family
Enterobacteriaceae, including strains of Escherichia coli, Salmonella typhimurium, Klebsiella pneumoniae, Shigella flexneri, and Enterobacter aerogenes. AZT also had bactericidal activity against Vibrio cholerae and the fish pathogen Vibrio anguillarum. AZT had no activity against Pseudomonas aeruginosa, gram-positive **bacteria**, anaerobic **bacteria**, Mycobacterium tuberculosis, nontuberculosis mycobacteria, or most fungal pathogens. Several lines of evidence indicated that AZT must be activated to the nucleotide level to **inhibit** cellular metabolism: (i) AZT was a substrate for E. coli thymidine kinase; (ii) spontaneously arising AZT-resistant mutants of E. coli ML-30 and S. typhimurium were deficient in thymidine kinase; and (iii) intact E. coli ML-30 cells converted [3H]AZT to its mono-, di-, and triphosphate metabolites. Of the phosphorylated metabolites, AZT-5'-triphosphate was the most potent **inhibitor** of replicative **DNA** synthesis in toluene-permeabilized E. coli pol A mutant cells. AZT-treated E. coli cultures grown in minimal medium contained highly elongated cells consistent with the **inhibition** of **DNA** synthesis. AZT-triphosphate was a specific **DNA** chain terminator in the in vitro **DNA** polymerization reaction catalyzed by the Klenow fragment of E. coli **DNA** polymerase I. Thus, **DNA** chain termination may explain the lethal properties of this compound against susceptible microorganisms.

L5 ANSWER 29 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 85027309 EMBASE
DOCUMENT NUMBER: 1985027309
TITLE: Further characterization of repair of 8-methoxypsoralen crosslinks in UV-excision-defective Escherichia coli.
AUTHOR: Bridges B.A.
CORPORATE SOURCE: MRC Cell Mutation Unit, University of Sussex, Falmer, Brighton, Sussex BN1 9RR, United Kingdom
SOURCE: Mutation Research, (1984) 132/5-6 (153-160).
CODEN: MUREAV
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
022 Human Genetics
013 Dermatology and Venereology
052 Toxicology
014 Radiology
030 Pharmacology
004 Microbiology
LANGUAGE: English
AB Evidence was previously presented for a new pathway for the repair of 8-methoxypsoralen **DNA** crosslinks. The pathway, which is independent of the uvrA gene but deficient in rep mutants, has now been further characterized and shown to be more active in minimal than in nutrient growth media and to be **inhibited** by acriflavine. Although crosslink repair is much reduced in recA bacteria, some still occurs as judged by the effect of acriflavine. By the same criterion, crosslink repair occurs in bacteria with point mutations in the uvR and uvrB genes, in bacteria with a deletion covering the uvrB gene, and in polA uvrA **bacteria**. **Bacteria** with insertions rather than point mutations in the uvrA gene, although showing evidence of repair, demonstrated minimal **inhibition** with acriflavine suggesting the possibility that the uvrA gene product, even if enzymically inactive, might be able to interact with **DNA** lesions in the

presence of acriflavine and **prevent** crosslink repair. Crosslink repair in E. coli WP2 uvrA is associated with base-pair substitution mutagenesis and may be characterized as an error-prone process. Crosslink repair in uvrA bacteria is reduced but not eliminated by a mutation in the umuC gene.

```
=> d his

     (FILE 'HOME' ENTERED AT 17:22:04 ON 19 FEB 2003)

     FILE 'CAPLUS, WPIDS, BIOSIS, MEDLINE, EMBASE' ENTERED AT 17:22:41 ON 19
     FEB 2003
L1         85846 "BACTERIA-TO-BACTERIA"
L2           384 L1 AND PLASMID AND GENES AND DNA
L3             7 L1 AND TAUROLIDINE
L4           202 L1(P)(PLASMID OR DNA)
L5            29 L4(P)(PREVENT? OR INHIBIT?)

=> logoff y
```

```
=> file caplus wpids biosis medline embase

FILE 'CAPLUS' ENTERED AT 16:55:36 ON 19 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 16:55:36 ON 19 FEB 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'BIOSIS' ENTERED AT 16:55:36 ON 19 FEB 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'MEDLINE' ENTERED AT 16:55:36 ON 19 FEB 2003

FILE 'EMBASE' ENTERED AT 16:55:36 ON 19 FEB 2003
COPYRIGHT (C) 2003 Elsevier Science B.V.  All rights reserved.

=> s plasmid(p)prevent?(p)bacteria(p)transfer?
L1          136 PLASMID(P) PREVENT?(P) BACTERIA(P) TRANSFER?

=> l1 and taurolidine
L2            0 L1 AND TAUROLIDINE

=> s "bacteria-to-bacteria transfer"
L3            0 "BACTERIA-TO-BACTERIA TRANSFER"

=> s "bacteria-to-bacteria"(p)transfer?(p)DNA
L4            9 "BACTERIA-TO-BACTERIA"(P) TRANSFER?(P) DNA

=> l1 and l4
L5            0 L1 AND L4

=> d l4 1-9 ibib ab

L4   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:90224  CAPLUS
DOCUMENT NUMBER:          136:129913
TITLE:                    Mutational analysis in isolation of regulated
                          virulence determinants of bacterial pathogens and the
                          rtxA and enhC genes from Legionella pneumophila
INVENTOR(S):              Cirillo, Jeffrey D.
PATENT ASSIGNEE(S):       The Board of Regents of the University of Nebraska,
                          USA
SOURCE:                   PCT Int. Appl., 131 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 2002008418      A2   20020131       WO 2001-US23306   20010724
     WO 2002008418      A3   20020613
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
```

VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-628871 A 20000724

AB The present invention relates to novel methods for isolation and identification of virulence determinants from bacterial pathogens. The present invention also relates to novel genes of the Legionella pneumophila bacteria, and methods of detection of Legionella pneumophila bacteria in samples. The present invention relates to novel methods for isolation and identification of virulence determinants from bacterial pathogens. A pool of bacterial mutants with enhanced virulence phenotype is obtained, and the **DNA** responsible as a factor for the enhanced virulence is located. Random mutations are inserted into the **DNA**, the **DNA transferred** into wild-type **bacteria**, and **bacteria** that no longer express the enhanced virulence are selected in order to identify an active site of the **DNA** necessary to confer enhanced virulence. The present invention also more specifically relates to novel rtxA and enhC genes of the Legionella pneumophila bacteria. Gene rtxA affects bacterial adherence to monocytes and epithelial cells, is involved in cytotoxicity and pore formation by L. pneumophila, and affects the bacterial virulence. These genes allow for the detection and quantitation of L. pneumophila and thus diagnosis of Legionnaires' disease, as well as for the design of inhibitors of the protein products of the genes.

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:110568 CAPLUS
DOCUMENT NUMBER: 135:206077
TITLE: Evidence for extensive resistance gene transfer among Bacteroides spp. and among Bacteroides and other genera in the human colon
AUTHOR(S): Shoemaker, N. B.; Vlamakis, H.; Hayes, K.; Salyers, A.
A.
CORPORATE SOURCE: Department of Microbiology, University of Illinois, Urbana, IL, 61801, USA
SOURCE: Applied and Environmental Microbiology (2001), 67(2), 561-568
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Transfer** of antibiotic resistance genes by conjugation is thought to play an important role in the spread of resistance. Yet virtually no information is available about the extent to which such horizontal **transfers** occur in natural settings. In this paper, we show that conjugal gene **transfer** has made a major contribution to increased antibiotic resistance in Bacteroides species, a numerically predominant group of human colonic bacteria. Over the past 3 decades, carriage of the tetracycline resistance gene, tetQ, has increased from about 30% to more than 80% of strains. Alleles of tetQ in different Bacteroides species, with one exception, were 96 to 100% identical at the **DNA** sequence level, as expected if horizontal gene **transfer** was responsible for their spread. Southern blot analyses showed further that **transfer** of tetQ was mediated by a conjugative transposon (CTn) of the CTnDOT type. Carriage of two

erythromycin resistance genes, ermF and ermG, rose from <2 to 23% and accounted for about 70% of the total erythromycin resistances obsd. Carriage of tetQ and the erm genes was the same in isolates taken from healthy people with no recent history of antibiotic use as in isolates obtained from patients with Bacteroides infections. This finding indicates that resistance **transfer** is occurring in the community and not just in clin. environments. The high percentage of strains that are carrying these resistance genes in people who are not taking antibiotics is consistent with the hypothesis that once acquired, these resistance genes are stably maintained in the absence of antibiotic selection. Six recently isolated strains carried ermB genes. Two were identical to erm(B)-P from Clostridium perfringens, and the other four had only one to three mismatches. The nine strains with ermG genes had **DNA** sequences that were more than 99% identical to the ermG of Bacillus sphaericus. Evidently, there is a genetic conduit open between gram-pos. **bacteria**, including **bacteria** that only pass through the human colon, and the gram-neg. Bacteroides species. Our results support the hypothesis that extensive gene **transfer** occurs among bacteria in the human colon, both within the genus Bacteroides and among Bacteroides species and gram-pos. bacteria.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:93810 CAPLUS
DOCUMENT NUMBER: 135:106091
TITLE: Bacteria-mediated DNA transfer for gene therapy and genetic vaccination
AUTHOR(S): Weiss, Siegfried; Chakraborty, Trinad
CORPORATE SOURCE: Molecular Immunology, GBF-National Research Center Biotechnol., Braunschweig, D-38124, Germany
SOURCE: Development of Novel Antimicrobial Agents: Emerging Strategies (2001), 81-89. Editor(s): Lohner, Karl. Horizon Scientific Press: Wymondham, UK. CODEN: 69AXXR
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review, with 25 refs. Transfer of eukaryotic expression plasmids to mammalian cells has recently been achieved using live attenuated bacteria. These successes have encouraged the use and generation of bacterial vector delivery systems that use local, mucosal and systemic routes of infection to deliver the desired gene directly to the cell type or organ of interest. Intrinsic properties of invasive bacteria such as their tropism for cell types or cell to cell spread are currently understood in great detail and provide the necessary basis for the design of novel vehicles. Finally, the ability of bacteria to harbor very large plasmids makes them very attractive as vehicles for gene therapy. Escherichia coli rendered artificially invasive and Listeria monocytogenes were used in vitro to transfer reporter genes into various types of cells from different species. Transfer could also be obsd. in vivo with L. monocytogenes albeit at low frequency. Shigella flexneri, Salmonella typhimurium and Salmonella typhi were used as vehicles to transfer plasmids for genetic immunization in vivo. Immune responses against the antigen encoded by the

expression plasmid could be detected in all cases. Thus, bacteria represent a simple and versatile carrier system for genetic immunization that should provide the flexibility required for the various vaccination problems. The low prodn. cost of such vaccines makes them attractive candidates for mass application.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:12666 CAPLUS
DOCUMENT NUMBER: 134:96206
TITLE: General method for isolation of regulated virulence determinants from bacterial pathogens and the rtxA and enhC genes from Legionella pneumophila
INVENTOR(S): Cirillo, Jeffrey D.
PATENT ASSIGNEE(S): The Board of Regents of the University of Nebraska, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000877	A2	20010104	WO 2000-US17743	20000627
WO 2001000877	A3	20020510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002086304	A1	20020704	US 2001-881901	20010615
US 2002086981	A1	20020704	US 2001-882583	20010615

PRIORITY APPLN. INFO.: US 1999-141717P P 19990630
US 2000-604561 A3 20000627

AB The present invention relates to novel methods for isolation and identification of virulence determinants from bacterial pathogens. A pool of bacterial mutants with enhanced virulence phenotype is obtained, and the **DNA** responsible as a factor for the enhanced virulence is located. Random mutations are inserted into the **DNA**, the **DNA transferred** into wild-type **bacteria**, and **bacteria** that no longer express the enhanced virulence are selected in order to identify an active site of the **DNA** necessary to confer enhanced virulence. The present invention also more specifically relates to novel rtxA and enhC genes of the Legionella pneumophila bacteria. Gene rtxA affects bacterial adherence to monocytes and epithelial cells, is involved in cytotoxicity and pore formation by L. pneumophila, and affects the bacterial virulence. These genes allow for the detection and quantitation of L. pneumophila and thus diagnosis of

Legionnaires' disease, as well as for the design of inhibitors of the protein products of the genes.

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1973:156890 CAPLUS
DOCUMENT NUMBER: 78:156890
TITLE: Transcription of spontaneously released bacterial deoxyribonucleic acid in frog auricles
AUTHOR(S): Stroun, Maurice; Anker, Philippe
CORPORATE SOURCE: Dep. Plant Physiol., Univ. Geneva, Geneva, Switz.
SOURCE: Journal of Bacteriology (1973), 114(1), 114-20
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB After frog auricles have been in contact with a suspension of **bacteria** of **bacteria**-free supernatant fluid, newly synthesized bacterial RNA is recovered in animal cells. Evidently the presence of bacterial **DNA**-dependent RNA polymerase is necessary for the transcription of bacterial **DNA** in the host cells. This seems to be related to a **transfer** of **DNA** and **DNA**-dependent RNA polymerase from bacteria into animal cells.

L4 ANSWER 6 OF 9 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1997-065167 [06] WPIDS
CROSS REFERENCE: 1995-240663 [31]
DOC. NO. CPI: C1997-021401
TITLE: Prodn. of heterologous non-bacterial protein in bacteria - using a chromosomal transfer DNA contg. a gene which has not been cloned in a multi-copy vector.
DERWENT CLASS: B04 D16
INVENTOR(S): MASCARENHAS, D; OLSON, P S; OLSON, P
PATENT ASSIGNEE(S): (CELT-N) CELTRIX PHARM INC
COUNTRY COUNT: 72
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9640722	A1	19961219	(199706)*	EN	80
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN					
AU 9659864	A	19961230	(199716)		
NO 9705748	A	19980119	(199813)		
CZ 9703944	A3	19980617	(199830)		
EP 859782	A1	19980826	(199838)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI					
AU 697444	B	19981008	(199901)		
NZ 309645	A	19981223	(199906)		
US 5861273	A	19990119	(199911)		
HU 9900868	A2	19990628	(199931)		
JP 11507521	W	19990706	(199937)		76
KR 99022717	A	19990325	(200024)		
CN 1190403	A	19980812	(200273)		
JP 3358818	B2	20021224	(200304)		42

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 9640722	A1	WO 1996-US9006	19960605
AU 9659864	A	AU 1996-59864	19960605
NO 9705748	A	WO 1996-US9006	19960605
		NO 1997-5748	19971205
CZ 9703944	A3	WO 1996-US9006	19960605
		CZ 1997-3944	19960605
EP 859782	A1	EP 1996-917207	19960605
		WO 1996-US9006	19960605
AU 697444	B	AU 1996-59864	19960605
NZ 309645	A	NZ 1996-309645	19960605
		WO 1996-US9006	19960605
US 5861273	A CIP of	US 1993-170588	19931221
		US 1995-482182	19950607
HU 9900868	A2	WO 1996-US9006	19960605
		HU 1999-868	19960605
JP 11507521	W	WO 1996-US9006	19960605
		JP 1997-501431	19960605
KR 99022717	A	WO 1996-US9006	19960605
		KR 1997-709159	19971208
CN 1190403	A	CN 1996-195423	19960605
JP 3358818	B2	WO 1996-US9006	19960605
		JP 1997-501431	19960605

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9659864	A	Based on	WO 9640722
CZ 9703944	A3	Based on	WO 9640722
EP 859782	A1	Based on	WO 9640722
AU 697444	B	Previous Publ.	AU 9659864
		Based on	WO 9640722
NZ 309645	A	Based on	WO 9640722
US 5861273	A	CIP of	US 5470727
HU 9900868	A2	Based on	WO 9640722
JP 11507521	W	Based on	WO 9640722
KR 99022717	A	Based on	WO 9640722
JP 3358818	B2	Previous Publ.	JP 11507521
		Based on	WO 9640722

PRIORITY APPLN. INFO: US 1995-482182 19950607; US 1993-170588 19931221

AB WO 9640722 A UPAB: 20030117

A method of producing a heterologous protein (A) comprises: (a) transferring a chromosomal DNA (I) into a bacterial host cell pref. comprising a chromosome, where (I) contains at least one copy of a gene encoding (A) and a selectable marker; (b) selecting for integration of (I) into the cell resulting in a host cell chromosome comprising a gene encoding (A) operably linked to a promoter functional in the host cell and a selectable marker flanked by duplicate DNA: and (c) expressing the gene, where the gene is at no time operably linked to a promoter, functional in the host cell, on a multicopy number plasmid vector during construction of the transfer DNA and where (A) accumulates within the host cell to a level in excess of 0.1% of total cell protein.

USE - The method is used to produce heterologous, pref. a non-bacterial, protein in a bacterial host cell such as E. coli to a level in excess of 1% of total cell protein. It is esp. useful for producing an eukaryotic esp. a mammalian protein.

ADVANTAGE - The method of construction avoids the generation of low or high multicopy plasmid where expression of a small amt. of the foreign protein may be toxic to the cell. The method allows high accumulation of the foreign protein (about 20% of total cell protein) from low (approx. 2) copies of the gene encoding (A).

Dwg.0/26

L4 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:151564 BIOSIS
DOCUMENT NUMBER: PREV200100151564
TITLE: Evidence for extensive resistance gene transfer among Bacteroides spp. and among Bacteroides and other genera in the human colon.
AUTHOR(S): Shoemaker, N. B.; Vlamakis, H.; Hayes, K.; Salyers, A. A. (1)
CORPORATE SOURCE: (1) Department of Microbiology, UIUC, 601 South Goodwin Ave., B103 CLSL, Urbana, IL, 61801: abigails@life.uiuc.edu USA
SOURCE: Applied and Environmental Microbiology, (February, 2001) Vol. 67, No. 2, pp. 561-568. print.
ISSN: 0099-2240.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Transfer** of antibiotic resistance genes by conjugation is thought to play an important role in the spread of resistance. Yet virtually no information is available about the extent to which such horizontal **transfers** occur in natural settings. In this paper, we show that conjugal gene **transfer** has made a major contribution to increased antibiotic resistance in Bacteroides species, a numerically predominant group of human colonic bacteria. Over the past 3 decades, carriage of the tetracycline resistance gene, tetQ, has increased from about 30% to more than 80% of strains. Alleles of tetQ in different Bacteroides species, with one exception, were 96 to 100% identical at the **DNA** sequence level, as expected if horizontal gene **transfer** was responsible for their spread. Southern blot analyses showed further that **transfer** of tetQ was mediated by a conjugative transposon (CTn) of the CTnDOT type. Carriage of two erythromycin resistance genes, ermF and ermG, rose from <2 to 23% and accounted for about 70% of the total erythromycin resistances observed. Carriage of tetQ and the erm genes was the same in isolates taken from healthy people with no recent history of antibiotic use as in isolates obtained from patients with Bacteroides infections. This finding indicates that resistance **transfer** is occurring in the community and not just in clinical environments. The high percentage of strains that are carrying these resistance genes in people who are not taking antibiotics is consistent with the hypothesis that once acquired, these resistance genes are stably maintained in the absence of antibiotic selection. Six recently isolated strains carried ermB genes. Two were identical to erm(B)-P from Clostridium perfringens, and the other four had only one to three mismatches. The nine strains with ermG genes had **DNA** sequences that were more than 99% identical to the ermG of Bacillus

sphaericus. Evidently, there is a genetic conduit open between gram-positive **bacteria**, including **bacteria** that only pass through the human colon, and the gram-negative Bacteroides species. Our results support the hypothesis that extensive gene **transfer** occurs among bacteria in the human colon, both within the genus Bacteroides and among Bacteroides species and gram-positive bacteria.

L4 ANSWER 8 OF 9 MEDLINE
ACCESSION NUMBER: 2001381324 MEDLINE
DOCUMENT NUMBER: 21091943 PubMed ID: 11157217
TITLE: Evidence for extensive resistance gene transfer among Bacteroides spp. and among Bacteroides and other genera in the human colon.
AUTHOR: Shoemaker N B; Vlamakis H; Hayes K; Salyers A A
CORPORATE SOURCE: Department of Microbiology, University of Illinois, Urbana, Illinois 61801, USA.
CONTRACT NUMBER: AI22383 (NIAID)
SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (2001 Feb) 67 (2) 561-8. Journal code: 7605801. ISSN: 0099-2240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB **Transfer** of antibiotic resistance genes by conjugation is thought to play an important role in the spread of resistance. Yet virtually no information is available about the extent to which such horizontal **transfers** occur in natural settings. In this paper, we show that conjugal gene **transfer** has made a major contribution to increased antibiotic resistance in Bacteroides species, a numerically predominant group of human colonic bacteria. Over the past 3 decades, carriage of the tetracycline resistance gene, tetQ, has increased from about 30% to more than 80% of strains. Alleles of tetQ in different Bacteroides species, with one exception, were 96 to 100% identical at the **DNA** sequence level, as expected if horizontal gene **transfer** was responsible for their spread. Southern blot analyses showed further that **transfer** of tetQ was mediated by a conjugative transposon (CTn) of the CTnDOT type. Carriage of two erythromycin resistance genes, ermF and ermG, rose from <2 to 23% and accounted for about 70% of the total erythromycin resistances observed. Carriage of tetQ and the erm genes was the same in isolates taken from healthy people with no recent history of antibiotic use as in isolates obtained from patients with Bacteroides infections. This finding indicates that resistance **transfer** is occurring in the community and not just in clinical environments. The high percentage of strains that are carrying these resistance genes in people who are not taking antibiotics is consistent with the hypothesis that once acquired, these resistance genes are stably maintained in the absence of antibiotic selection. Six recently isolated strains carried ermB genes. Two were identical to erm(B)-P from Clostridium perfringens, and the other four had only one to three mismatches. The nine strains with ermG genes had **DNA** sequences that were more than 99% identical to the ermG of Bacillus sphaericus. Evidently, there is a genetic conduit open between

gram-positive **bacteria**, including **bacteria** that only pass through the human colon, and the gram-negative Bacteroides species. Our results support the hypothesis that extensive gene **transfer** occurs among bacteria in the human colon, both within the genus Bacteroides and among Bacteroides species and gram-positive bacteria.

L4 ANSWER 9 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001053313 EMBASE
TITLE: Evidence for extensive resistance gene transfer among Bacteroides spp. and among Bacteroides and other genera in the human colon.
AUTHOR: Shoemaker N.B.; Vlamakis H.; Hayes K.; Salyers A.A.
CORPORATE SOURCE: A.A. Salyers, Department of Microbiology - UIUC, B103 CLSL,
601 South Goodwin Ave., Urbana, IL 61801, United States.
abigails@life.uiuc.edu
SOURCE: Applied and Environmental Microbiology, (2001) 67/2 (561-568).
Refs: 52
ISSN: 0099-2240 CODEN: AEMIDF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Transfer** of antibiotic resistance genes by conjugation is thought to play an important role in the spread of resistance. Yet virtually no information is available about the extent to which such horizontal **transfers** occur in natural settings. In this paper, we show that conjugal gene **transfer** has made a major contribution to increased antibiotic resistance in Bacteroides species, a numerically predominant group of human colonic bacteria. Over the past 3 decades, carriage of the tetracycline resistance gene, tetQ, has increased from about 30% to more than 80% of strains. Alleles of tetQ in different Bacteroides species, with one exception, were 96 to 100% identical at the **DNA** sequence level, as expected if horizontal gene **transfer** was responsible for their spread. Southern blot analyses showed further that **transfer** of tetQ was mediated by a conjugative transposon (CTn) of the CTnDOT type. Carriage of two erythromycin resistance genes, ermF and ermG, rose from <2 to 23% and accounted for about 70% of the total erythromycin resistances observed. Carriage of tetQ and the erm genes was the same in isolates taken from healthy people with no recent history of antibiotic use as in isolates obtained from patients with Bacteroides infections. This finding indicates that resistance **transfer** is occurring in the community and not just in clinical environments. The high percentage of strains that are carrying these resistance genes in people who are not taking antibiotics is consistent with the hypothesis that once acquired, these resistance genes are stably maintained in the absence of antibiotic selection. Six recently isolated strains carried ermB genes. Two were identical to erm(B)-P from Clostridium perfringens, and the other four had only one to three mismatches. The nine strains with ermG genes had **DNA** sequences that were more than 99% identical to the ermG of Bacillus sphaericus. Evidently, there is a genetic conduit open between gram-positive **bacteria**, including **bacteria** that only pass through the human colon, and the gram-negative Bacteroides species. Our results support the hypothesis that extensive gene **transfer** occurs among bacteria in the human colon, both within the genus

Bacteroides and among Bacteroides species and gram-positive bacteria.

```
=> l4 and taurolidine
L6            0 L4 AND TAUROLIDINE

=> d his

     (FILE 'HOME' ENTERED AT 16:55:01 ON 19 FEB 2003)

     FILE 'CAPLUS, WPIDS, BIOSIS, MEDLINE, EMBASE' ENTERED AT 16:55:36 ON 19
     FEB 2003
L1          136 S PLASMID(P)PREVENT?(P)BACTERIA(P)TRANSFER?
L2            0 L1 AND TAUROLIDINE
L3            0 S "BACTERIA-TO-BACTERIA TRANSFER"
L4            9 S "BACTERIA-TO-BACTERIA"(P)TRANSFER?(P)DNA
L5            0 L1 AND L4
L6            0 L4 AND TAUROLIDINE

=> logoff y
```

```
show files
File 155:MEDLINE(R) 1966-2002/Aug W3
File   5:Biosis Previews(R) 1969-2002/Aug W2
         (c) 2002 BIOSIS
File 315:ChemEng & Biotec Abs 1970-2002/Jul
         (c) 2002 DECHEMA
File  73:EMBASE 1974-2002/Aug W3
         (c) 2002 Elsevier Science B.V.
?ds

Set     Items   Description
S1         94   AU=COSTIN J? OR AU=COSTIN, J?
S2        374   TAUROLIDINE
S3        174   TAUROLIN?
S4        886   THIADIAZINE?
S5       1323   METHYLENEBIS?
S6    1075708   RESISTAN?
S7     228365   STAPH?
S8      38984   VANCOMYCIN
S9     827907   TRANSFER?
S10    441220   PLASMID? OR VECTOR? ?
S11   2667214   BACTERI?
S12    399891   ADHES? OR ADHER?
S13         2   S1 AND (S2 OR S3 OR (S4(5N)S5))
S14       423   (S2 OR S3 OR (S4(5N)S5))
S15        20   S14 AND (S6(5N)(ANTIBIOTIC? ? OR VANCOMYCIN))
S16        15   S14 AND S7 AND S6
S17         2   S14 AND S10
S18        27   S15-S17
S19        29   S13 OR S15-S17
S20        21   RD S19 (unique items)
?t 20/7/all

 20/7/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13308217   22001262   PMID: 12006145
  A randomized double-blinded placebo-controlled crossover trial of
nebulized taurolidine in adult cystic fibrosis patients infected with
Burkholderia cepacia.
  Ledson Martin J; Gallagher Malcolm J; Robinson Maxine; Cowperthwaite
Carolyn; Williets Trevor; Hart Charles A; Walshaw Martin J
  Regional Adult Cystic Fibrosis Unit, Liverpool University, Liverpool,
United Kingdom.
  Journal of aerosol medicine : the official journal of the International
Society for Aerosols in Medicine (United States)  Spring 2002,  15  (1)
 p51-7,  ISSN 0894-2684   Journal Code: 8809251
  Document type: Clinical Trial; Journal Article; Randomized Controlled
Trial
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Burkholderia cepacia is an aggressive pathogen that colonizes cystic
fibrosis (CF) patients, causing greatly increased morbidity and mortality.
It is resistant to most antibiotics , but sensitive in vitro to a novel
agent, taurolidine . This has not previously been used against B. cepacia,
nor given in nebulized form. We assessed the effect of nebulized
```

taurolidine on United Kingdom epidemic (ET12) B. cepacia infection in 20 adult CF patients attending our regional adult cystic fibrosis outpatient clinic using a prospective, randomized, double-blinded placebo-controlled crossover trial. Nebulized taurolidine (4 mL 2% solution) or saline (4 mL 0.9% solution) was given twice daily. Each arm lasted 4 weeks, with a 2-week intervening washout period. Sputum B. cepacia colony counts (primary outcome measure), spirometry, and symptoms (secondary outcome measures) were assessed. Eighteen patients completed the study. There was no change in B. cepacia colony counts or spirometry, nor symptom scores. We conclude that, although taurolidine is well tolerated in nebulized form, in this study it had no in vivo anti-B. cepacia activity.
Record Date Created: 20020513

20/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10732600 20277911 PMID: 10817739
Activities of taurolidine in vitro and in experimental enterococcal endocarditis.
Torres-Viera C; Thauvin-Eliopoulos C; Souli M; DeGirolami P; Farris M G; Wennersten C B; Sofia R D; Eliopoulos G M
Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts 02115, USA.
Antimicrobial agents and chemotherapy (UNITED STATES) Jun 2000, 44 (6) p1720-4, ISSN 0066-4804 Journal Code: 0315061
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In vitro, the antimicrobial agent taurolidine inhibited virtually all of the bacteria tested, including vancomycin - resistant enterococci, oxacillin- resistant staphylococci , and Stenotrophomonas maltophilia, at concentrations between 250 and 2,000 microg/ml. Taurolidine was not effective in experimental endocarditis. While it appears unlikely that this antimicrobial would be useful for systemic therapy, its bactericidal activity and the resistance rates found (<10(-9)) are favorable indicators for its possible development for topical use.
Record Date Created: 20000711

20/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09516741 97411522 PMID: 9333700
1996 pathogen incidence and resistance status in peritonitis]
Erregerhaufigkeit und Resistenzsituation bei Peritonitis 1996.
Focht J; Nosner K
Institut fur Laboruntersuchungen, Moers.
Langenbecks Archiv fur Chirurgie (GERMANY) 1997, 382 (4 Suppl 1) pS1-4, ISSN 0023-8236 Journal Code: 0204167
Document type: Journal Article ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed
Severe intra-abdominal infection is associated with a high mortality rate. In addition to risk factors in the patients, the causal pathogens and

the selection of appropriate therapeutic procedures play an essential part in the course of these conditions. In the majority of intra-abdominal infections mixed aerobic/anaerobic infections, mostly with some involvement of enterobacteria and also of enterococci and staphylococci can be demonstrated. In addition to surgical intervention a calculated antimicrobial initial treatment of intra-abdominal infections with an antibiotic with an adequate effect to combat the pathogen concerned can contribute to improving the patient's prognosis. A calculated antibiotic treatment can only be effectively and reliably carried through if the frequency of the pathogen and the resistance situation are known. Retrospective evaluations of data on the sensitivity and frequency of pathogens from a defined group of subjects allow conclusions on the epidemiological situation in a particular catchment area or in a medical sector and thus make it possible to calculate the appropriate therapy for infections. In 1996 a total of 2,779 bacterial isolates from the intra-abdominal infection sector were examined: 935 Enterobacteriaceae, 83 nonfermenters, 177 Staphylococcus spp., 211 Enterococcus spp., 39 Streptococcus spp., and 1334 different anaerobic bacteria. Fresh clinical isolates were available for all pathogens tested. The most frequent gram-negative pathogen was E. coli (60%) and the most frequent gram-positive pathogen, E. faecalis (44%); the most frequent anaerobic pathogen was B. fragilis (39%). Taurolodine had the lowest resistance rate against gram-negative and anaerobic pathogens. Teicoplanin had the highest activity against gram-positive pathogens.

Record Date Created: 19971015

20/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07848858 93380383 PMID: 8370323

Taurolidine : in vitro activity against multiple- antibiotic - resistant , nosocomially significant clinical isolates of Staphylococcus aureus, Enterococcus faecium, and diverse Enterobacteriaceae.

Traub W H; Leonhard B; Bauer D

Institut fur Medizinische Mikrobiologie und Hygiene, Universitat des Saarlandes, Homburg/Saar, BRD.

Chemotherapy (SWITZERLAND) Sep-Oct 1993, 39 (5) p322-30, ISSN 0009-3157 Journal Code: 0144731

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Taurolidine at < or = 1,250 micrograms/ml killed all 37 isolates of multiple- antibiotic - resistant Staphylococcus aureus (n = 9), Enterococcus faecium (n = 17), and Enterobacteriaceae (n = 11). Time-kill experiments disclosed that bovine serum (65% v/v) only marginally retarded the bactericidal activity of 2,000 and 1,000 micrograms/ml of taurolidine against the various strains. Taurolidine at 2,000 micrograms/ml did not antagonize the bactericidal activity of 50% (v/v) fresh human serum against promptly and delayed serum-sensitive test strains of Escherichia coli and Serratia marcescens. In the presence of 65% (v/v) of fresh defibrinated human blood from two donors, however, the bactericidal activity of this antimicrobial compound was delayed, i.e., manifested only following extended (overnight) incubation, against staphylococcal and enterococcal isolates, though less so in the case of Enterobacteriaceae. Taurolidine at 2,000 micrograms/ml killed ingested, i.e., intraphagocytic bacteria of

human-serum- resistant S. marcescens strains CDC 06:H3 and P016:H-.
Record Date Created: 19931008

20/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07788337 93314363 PMID: 8325127
Enterococcus faecium: in vitro activity of antimicrobial drugs, singly and combined, with and without defibrinated human blood, against multiple-antibiotic - resistant strains.
Traub W H; Leonhard B; Bauer D
Institut fur Medizinische Mikrobiologie und Hygiene, Universitat des Saarlandes, Homburg/Saar, BRD.
Chemotherapy (SWITZERLAND) Jul-Aug 1993, 39 (4) p254-64, ISSN 0009-3157 Journal Code: 0144731
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The minimal inhibitory (MICs) and bactericidal concentrations of 14 antimicrobial drugs were determined against 17 clinical isolates of Enterococcus faecium, including 4 glycopeptide- resistant strains. Both teicoplanin and vancomycin lacked bactericidal activity against all 13 susceptible isolates. Time-kill experiments served to test various antibiotic combinations chiefly against glycopeptide- resistant strains in Mueller-Hinton broth (MHB) and in MHB supplemented with 65% (v/v) fresh defibrinated human blood. Co-trimoxazole, fusidic acid, and novobiocin yielded bacteriostatic effects. Rifampin was bactericidally active against rifampin-susceptible strains (MICs = 0.125 micrograms/ml), but less so against low-level-rifampin-resistant (MICs = 2-8 micrograms/ml) strains in MHB. However, in the presence of human blood, rifampin (2 micrograms/ml) combined with co-trimoxazole (0.25/4.75 micrograms/ml) killed rifampin-susceptible and low-level-rifampin-resistant, but not moderate-level-rifampin-resistant (MICs = 16-32 micrograms/ml) strains of E. faecium. Of two topical drugs examined, mupirocin merely inhibited strains of E. faecium; conversely, taurolidine at 2,000 micrograms/ml was efficacious against all strains examined, although the kinetics of bactericidal activity were retarded somewhat in the presence of 65 vol% human blood.
Record Date Created: 19930810

20/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06623499 90324089 PMID: 2197257
[Value of systemic and local administration of antibiotics in soft tissue and bone infections]
Stellenwert systemischer und lokaler Antibiotika-Anwendung bei Weichteil- und Knocheninfekten.
Rittmann W W; Schawalder K; Enzler M
Klinik fur Chirurgie, Kantonsspital St. Gallen.
Helvetica chirurgica acta (SWITZERLAND) Apr 1990, 56 (6) p879-89, ISSN 0018-0181 Journal Code: 2985095R
Document type: Journal Article; Review; Review, Tutorial ; English Abstract

Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed

There is little data to support the efficacy of prophylactic antibiotics in traumatology. In closed fractures three randomized controlled studies using a 1-3 day prophylaxis with Cephalosporins of the first or second generation or a Penicillinase-resistent Penicillin demonstrated a reduction of the infection rate. For the Cephalosporins of the second generation it was shown, that a single dose was less efficient than five repeated applications over 24 hours. In hip-fractures a prophylaxis with Cephalothin or Cefotiam reduced the frequency of infections when compared with controls. In open fractures a treatment over 10 days using Cephalothin or Isoxazolyl-Penicillin showed a significant drop of the infection rate. If however the fractures were not treated using the principles of rigid internal fixation and were covered with Dicloxacillin over 2 days only there was no significant improvement. A multicenter study finally indicates that a one day course of cefonicid sodium is not inferior to a prolonged course of antibiotics for prevention of early postoperative fracture-site infections. We conclude, that open and closed fractures can profit from antibiotic prophylaxis which starts immediately before surgery and is continued over 24 hours. We favour Isoxazolyl-Penicillin because of its efficacy against staphylococcus aureus and epidermidis which predominate in early infection. In established bone and soft tissue infections antibiotics are used when there is local spreading, sepsis, involvement of joints or when reinterventions in the infectious focus are necessary. In these cases bacteriological testing in the laboratory is essential for the selection of antibiotics. Local application of antibiotics in irrigation-drainage solutions can not be recommended. PMMA-chains serve as temporary spacers, but should be removed early before their extraction becomes difficult and resistant bacteria develop. When defects are closed with cancellous bone or soft tissues the use of Gentamycin-fleece or Taurolin -gels is recommended. (9 Refs.)

Record Date Created: 19900824

20/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03502043 81036513 PMID: 6107015

Nebacetin and taurolin as intraoperative disinfectant solutions in surgery of the locomotor system (author's transl)]

Nebacetin und Taurolin als intraoperative Spullosungen bei Eingriffen am Bewegungsapparat.

Burri C; Lob G; Rudzki M

Aktuelle Traumatologie (GERMANY, WEST) Apr 1980, 10 (2) p65-72, ISSN 0044-6173 Journal Code: 0421405

Document type: Journal Article ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed

The anti-infective preventive action of intraoperative disinfection with physiological solution containing antibiotics, appears to be firmly established, judging from numerous publications. Since germs are showing a world-wide increasing resistance , the search for antibiotics which continue to be effective must be kept up, but alternative suggestions are equally necessary. Some publications have already been presented indicating that success similar to that previously obtained with antibiotics is

possible by using disinfectants in the prophylaxis and treatment of infections. Hence, a comparative study was conducted using the non-absorbable broad-spectrum antibiotic Nebacetin and the disinfectant Taurolin in a 1% solution with a group of patients subjected to a total of 7699 major and minor surgical operations. Prospectively, early infections during the stay of the patient in the hospital, als well as disturbed wound healing, were included. No significant difference was found in the number of infections and the rate of disturbed wound healing. Indirectly, it is possible to conclude with the help of results from literature that the disinfectant Taurolin is suitable as an addition to intra-operative rinsing in the prophylaxis of infections.
Record Date Created: 19801216

20/7/8 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13671063 BIOSIS NO.: 200200299884
Stability and efficacy of antibiotic-anticoagulant lock solutions for central venous catheter-related sepsis.
AUTHOR: Droste Jan C(a); Farrington Ken(a); Macdonald Alan; Jeraj Hassan A
AUTHOR ADDRESS: (a)Renal Medicine, Lister Hospital, Stevenage**UK
JOURNAL: Journal of the American Society of Nephrology 12 (Program and Abstract Issue):p376A September, 2001
MEDIUM: print
CONFERENCE/MEETING: ASN (American Society of Nephrology)/ISN (International Society of Nephrology) World Congress of Nephrology San Francisco, CA, USA October 10-17, 2001
ISSN: 1046-6673
RECORD TYPE: Citation
LANGUAGE: English

20/7/9 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13649297 BIOSIS NO.: 200200278118
Compositions and methods for treating infections of the ear.
AUTHOR: Costin James C (a
AUTHOR ADDRESS: (a)Lower Gwynedd, PA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1255 (4):pNo Pagination Feb. 26, 2002
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The use of 4,4- methylenebis (tetrahydro-1,2,4- thiadiazine -1,2-dioxide) in treating infections of the ear.

20/7/10 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13575513 BIOSIS NO.: 200200204334
Prevention of hemodialysis catheter-related bloodstream infection using an antimicrobial lock.
AUTHOR: Quarello Francesco(a); Forneris Giacomo
AUTHOR ADDRESS: (a)Divisione di Nefrologia e Dialisi, Ospedale San Giovanni Bosco, Piazza Donatore di Sangue, 3, I-10154, Torino**Italy E-Mail: fquarello@tin.it
JOURNAL: Blood Purification 20 (1):p87-92 2002
MEDIUM: print
ISSN: 0253-5068
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Among currently available vascular access options for hemodialysis, central venous catheters show the poorest reliability, with frequent complications of thrombosis and stenosis impairing patency. The most serious problem, however, is catheter-related bloodstream infection (CRBI), which is typically a cause for removal of the catheter and protracted systemic antibiotic therapy. In our experience, a totally implanted device (Dialock(R), Biolink Corp.) seems to confer a better global protection against catheter-related infections than standard tunneled catheters, accounting for 0.97 vs. 4.75 infection episodes/1,000 catheter-days, respectively ($p<0.001$). Bloodstream infection rates, however, are not statistically different in the two groups (0.85 vs. 0.81 per 1,000 catheter-days; p=n.s.), indicating that the improvement is mainly related to local cutaneous infections. On the other hand, in the Sodemann experience, a new taurolidine -based lock solution (Neutrolin(R), Biolink Corp.) greatly reduced CRBI rates with both subcutaneous ports and tunneled catheters to 0.29 and 0.20 episodes/1,000 catheter-days, respectively. These promising results await further confirmation from ongoing clinical trials.

20/7/11 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13209918 BIOSIS NO.: 200100417067
Compositions and methods for the management of Crohn's disease.
AUTHOR: Costin James C (a
AUTHOR ADDRESS: (a)Belle Mead, NJ**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1247 (4):pNo Pagination June 26, 2001
MEDIUM: e-file
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The present invention relates to a method of treating a human infected with Crohn's disease comprising enterally administering to the individual in need of such treatment an effective amount of a composition comprising 4,4'- methylenebis -(tetrahydro-1,2,4- thiadiazine)-1,1,1',1'-tetraoxide, commonly known as taurolidine .

20/7/12 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11577809 BIOSIS NO.: 199800358505
Taurolidine 2 percent as an antimicrobial lock solution for prevention of recurrent catheter-related bloodstream infections.
AUTHOR: Jurewitsch Brian(a); Lee Tundra; Park Joan; Jeejeebhoy Khursheed
AUTHOR ADDRESS: (a)Dep. Pharmacy, St. Michael's Hosp., Toronto, ON M5B 1W8 **Canada
JOURNAL: Journal of Parenteral and Enteral Nutrition 22 (4):p242-244 July-Aug., 1998
ISSN: 0148-6071
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: This case report describes our preliminary data on the use of taurolidine as a lock technique. Taurolidine is a novel antimicrobial agent that has found a niche in Europe for prevention of bacteremia in home parenteral nutrition (HPN) patients who have multiple catheter-related bloodstream infections. Methods: A 29-year-old male with short bowel syndrome was admitted 18 times in 9 years for treatment of Gram-positive, Gram-negative, and yeast-associated catheter-related bloodstream infections. Management consisted of conventional antibiotic treatment in accordance with blood culture and sensitivity results as well as catheter removal in 10 cases. Ten months before the last infection, the patient was instructed to instil 1.5 mL taurolidine 2% daily into his central line after finishing his HPN infusion and has continued to do so 2 years to date. Results: The incidence of catheter-related bloodstream infections decreased from 8.5 to 1.5 infections per 1000 catheter days. Conclusions: These data support previous observations made outside North America and suggest that taurolidine may prove to be an effective and safe antimicrobial agent for the prevention of recurrent catheter-related bloodstream infections.

20/7/13 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11087302 BIOSIS NO.: 199799708447
Spectrum of pathogens and resistance in peritonitis.
AUTHOR: Focht J(a); Noesner K
AUTHOR ADDRESS: (a)Biosci., Inst. Laboruntersuchungen, Zum Schuermannsgraben 30, D-47441 Moers**Germany
JOURNAL: Langenbecks Archiv fuer Chirurgie 382 (4 SUPPL. 1):pS1-S4 1997
ISSN: 0023-8236
RECORD TYPE: Abstract
LANGUAGE: German; Non-English
SUMMARY LANGUAGE: German; English

ABSTRACT: Severe intra-abdominal infection is associated with a high mortality rate. In addition to risk factors in the patients, the causal pathogens and the selection of appropriate therapeutic procedures play an essential part in the course of these conditions. In the majority of

intra-abdominal infections mixed aerobic/anaerobic infections, mostly with some involvement of enterobacteria and also of enterococci and staphylococci can be demonstrated. In addition to surgical intervention a calculated antimicrobial initial treatment of intra-abdominal infections with an antibiotic with an adequate effect to combat the pathogen concerned can contribute to improving the patient's prognosis. A calculated antibiotic treatment can only be effectively and reliably carried through if the frequency of the pathogen and the resistance situation are known. Retrospective evaluations of data on the sensitivity and frequency of pathogens from a defined group of subjects allow conclusions on the epidemiological situation in a particular catchment area or in a medical sector and thus make it possible to calculate the appropriate therapy for infections. In 1996 a total of 2,779 bacterial isolates from the intra-abdominal infection sector were examined: 935 Enterobacteriaceae, 83 nonfermenters, 177 Staphylococcus spp., 211 Enterococcus spp., 39 Streptococcus spp., and 1334 different anaerobic bacteria. Fresh clinical isolates were available for all pathogens tested. The most frequent gram-negative pathogen was E. coli (60%) and the most frequent gram-positive pathogen, E. faecalis (44%); the most frequent anaerobic pathogen was B. fragilis (39%). Taurolodine had the lowest resistance rate against gram-negative and anaerobic pathogens. Teicoplanin had the highest activity against gram-positive pathogens.

20/7/14 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02152387 BIOSIS NO.: 000063067390
TAUROLIN A NEW CHEMO THERAPEUTIC AGENT
AUTHOR: BROWNE M K; LESLIE G B; PFIRRMANN R W
JOURNAL: J APPL BACTERIOL 41 (3). 1976 (RECD 1977) 363-368. 1976
FULL JOURNAL NAME: Journal of Applied Bacteriology
CODEN: JABAA
RECORD TYPE: Abstract

ABSTRACT: Taurolin , bis-(1,1-dioxo-perhydro-1,2,4-thiadiazinyl-4)-methan, is a novel, broad spectrum, nonsystemic chemotherapeutic agent. It is effective in vivo against a wide range of pathogenic organisms including Pseudomonas aeruginosa, Escherichia coli, Proteus vulgaris and Salmonella typhimurium, and would be of particular use against antibiotic - resistant organisms. It is based on an endogenous substance, taurine, which acts as a non-toxic formaldehyde carrier donating methylol groups to bacterial protein and endotoxin thus causing denaturation and polycondensation of the pathogens and their pyrogens. Taurolin may be of value in the treatment of fecal peritonitis.

20/7/15 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11615278 EMBASE No: 2002182965
Antimicrobial activity of a novel catheter lock solution
Shah C.B.; Mittelman M.W.; Costerton J.W.; Parenteau S.; Pelak M.; Arsenault R.; Mermel L.A.
L.A. Mermel, Division of Infectious Diseases, Rhode Island Hospital, 593

Eddy St., Providence, RI 02903 United States
AUTHOR EMAIL: lmermel@lifespan.org
Antimicrobial Agents and Chemotherapy (ANTIMICROB. AGENTS CHEMOTHER.) (United States) 2002, 46/6 (1674-1679)
CODEN: AMACC ISSN: 0066-4804
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 28

Intravascular catheter-associated bloodstream infections significantly increase rates of morbidity and hospital costs. Microbial colonization and development of biofilms, which are known to be recalcitrant to antibiotic therapy, often lead to the loss of otherwise patent vascular access systems. We evaluated a new taurolidine - and citrate-based catheter lock solution (Neutrolin; Biolink Corporation, Norwell, Mass.) for its activity against planktonic microbes, antimicrobial activity in a catheter model, and biofilm eradication activity. In studies of planktonic microbes, after 24 h of contact, 675 mg of taurolidine -citrate solution per liter caused >99% reductions in the initial counts of Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, and Entercoccus faecalis. A solution of 13,500 mg/liter was cidal for Candida albicans. Ports and attached catheters inoculated with 50 to 600 CFU of these bloodstream isolates per ml were locked with heparin or the taurolidine -citrate solution. After 72 h, there was no growth in the taurolidine -citrate-treated devices but the heparin-treated devices exhibited growth in the range of 6 x 10SUP2 to 5 x 10SUP6 CFU/ml. Biofilms were developed on silicone disks in modified Robbins devices with broth containing 6% serum (initial counts, 10SUP6 to 10SUP8 CFU/cmSUP2). The axenic biofilms were treated for 24 h with taurolidine -citrate or heparin. Taurolidine -citrate exposure resulted in a median reduction of 4.8 logs, whereas heparin treatment resulted in a median reduction of 1.7 logs ($P < 0.01$). No significant differences in the effects of the two treatments against P. aeruginosa and C. albicans were observed. These findings suggest that taurolidine -citrate is a promising combination agent for the prevention and treatment of intravascular catheter-related infections.

20/7/16 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11193813 EMBASE No: 2001203139
Therapy of infection
Rommes J.H.; Rios G.; Zandstra D.F.
J.H. Rommes, Department of Intensive Care, Gelre Ziekehuizen, PO Box 9014, 7300 DS Apeldoorn Netherlands
Current Anaesthesia and Critical Care (CURR. ANAESTH. CRIT. CARE) (United Kingdom) 2001, 12/1 (25-33)
CODEN: CCCAE ISSN: 0953-7112
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 51

The five basic principles behind the concept of the treatment of an established infection are as follows: (1) surveillance and diagnostic cultures to ensure identification of the micro-organism so that modification of the otherwise 'blind' treatment can be undertaken; (2)

immediate and adequate antibiotic treatment in order to sterilize the infected internal organs; (3) the source of potential pathogens causing the infection - whether endogenous or exogenous - requires elimination for both the recovery of the original infection and the prevention of relapses and/or superinfections. Selective decontamination of the digestive tract (SDD) aims at the eradication of internal sources of the oropharynx and gut in patients, whilst identification and eradication of the external sources outside the patients, using disposables and/or hygiene, are an integral part of the therapy of infection; (4) removal or replacement of invasive devices often contaminated with the potential pathogen is thought to contribute to the healing in curtailing the supply of micro-organisms; (5) surveillance samples are indispensable in evaluating the efficacy of this five component protocol. The treatment of practically all infections relies on these five basics, in particular lower airway and blood stream infections developing in the critically ill requiring intensive care including mechanical ventilation. Special attention is given in this chapter to the under-estimated problem of exogenous infections due to intensive care unit (ICU) associated bacteria without preceding carriage, and to the increasing problem of the serious infections caused by methicillin- resistant Staphylococcus aureus (MRSA).

20/7/17 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

06928072 EMBASE No: 1997212551
Therapy of severe visceral infections
THERAPIE VON SCHWEREN VISZERALEN INFEKTIONEN
Gabler-Sandberger E.
Notfall Medizin (NOTF. MED.) (Germany) 1997, 23/5 (184)
CODEN: NOMED ISSN: 0341-2903
DOCUMENT TYPE: Journal; Note
LANGUAGE: GERMAN

20/7/18 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

05470631 EMBASE No: 1993238730
Taurolidine : In vitro activity against multiple- antibiotic resistantl nosocomially significant clinical isolates of staphylococcus aureus enterococcus faecium, and diverse enterobacteriaceae
Traub W.; Leonhard B.; Bauer D.
Inst fur Medizinische Mikrobiologie, Haus 43,D-66421 Homburg/Saar Germany
Chemotherapy (CHEMOTHERAPY) (Switzerland) 1993, 39/5 (322-330)
CODEN: CHTHB ISSN: 0009-3157
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Taurolidine at <= 1,250 mug/ml killed all 37 isolates of multiple-antibiotic - resistant Staphylococcus aureus (n = 9), Enterococcus faecium (n = 17), and Enterobacteriaceae (n = 11). Timekill experiments disclosed that bovine serum (65% v/v) only marginally retarded the

bactericidal activity of 2,000 and 1,000 mug/ml of taurolidine against the various strains. Taurolidine at 2,000 mug/ml did not antagonize the bactericidal activity of 50% (v/v) fresh human serum against promptly and delayed serumsensitive test strains of Escherichia coli and Serratia marcescens. In the presence of 65% (v/v) of fresh defibrinated human blood from two donors, however, the bactericidal activity of this antimicrobial compound was delayed, i.e., manifested only following extended (overnight) incubation, against staphylococcal and enterococcal isolates, though less so in the case of Enterobacteriaceae. Taurolidine at 2,000 mug/ml killed ingested, i.e., intraphagocytic bacteria of human-serum- resistant S. marcescens strains CDC 06:H3 and P 016:H-.

20/7/19 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

05307599 EMBASE No: 1993075684
Factors influencing the adhesion of uropathogens to the uroepithelium
Reid G.; Bruce A.W.
Research Services, SLB 328, University of Western Ontario,London, Ont. N6A 5B8 Canada
Current Opinion in Urology (CURR. OPIN. UROL.) (United Kingdom) 1993, 3/1 (21-24)
CODEN: CUOUE ISSN: 0963-0643
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

20/7/20 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

01634630 EMBASE No: 1980129105
Nebacetin(R) and taurolin as intra-operative disinfectant solutions in surgery of the locomotor system
NEBACETIN(R) UND TAUROLIN ALS INTRAOPERATIVE SPULLOSUNGEN BEI EINGRIFFEN AM BEWEGUNGSAPPARAT
Burri C.; Lob G.; Rudzki M.
Abt. Unfallchir. Plastische Wiederherstellungschir., Univ. Ulm Germany
Aktuelle Traumatologie (AKTUEL. TRAUMATOL.) (Germany) 1980, 10/2 (65-72)
CODEN: AKTRA
DOCUMENT TYPE: Journal
LANGUAGE: GERMAN SUMMARY LANGUAGE: ENGLISH

The anti-infective preventive action of intra-operative disinfection with physiological solution containing antibiotics, appears to be firmly established, judging from numerous publications. Since germs are showing a world-wide increasing resistance , the search for antibiotics which continue to be effective must be kept up, but alternative suggestions are equally necessary. Some publications have already been presented indicating that success similar to that previously obtained with antibiotics is possible by using disinfectants in the prophylaxis and treatment of infections. Hence, a comparative study was conducted using the non-absorbable broad-spectrum antibiotic Nebacetin(R) and the disinfectant taurolin in a 1% solution with a group of patients subjected to a total of

7699 major and minor surgical operations. Prospectively, early infections during the stay of the patient in the hospital, as well as disorder in the healing of the wound, were included. No significant difference was found in the number of infections and the rate of disorders in the healing of the wound. Indirectly, it is possible to conclude with the help of results from the literature that the disinfectant taurolin is suitable as an addition to intra-operative rinsing in the prophylaxis of infections.

20/7/21 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

01374980 EMBASE No: 1979095680
Antibiotic therapy in acute peritonitis
LE TRAITEMENT ANTIBIOTIQUE AU COURS DES PERITONITES AIGUES
Gouin F.; Raybaud F.; Auffray J.P.; Viard L.
Dept. Anesth. Reanim. Marseille-Sud, 13009 Marseille France
Annales de l'Anesthesiologie Francaise (ANN. ANESTHESIOL. FR.) (France)
1978, 19/11-12 (915-918)
CODEN: AANFA
DOCUMENT TYPE: Journal
LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH
?logoff hold